ABCD

Med Trib 10

Medical Tribune

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and Medical News

Vol. 16, No. 10 — world news of medicine and its practice—fast, accurate, complete — Wednesday, March 12, 1975

making rounds at press time

"CONSTRUCTIVE OFFERS" by individual hoapitals in N.Y.C.'s League of Voluntary Hospitals hsve been made to the Committee of Interns and Residents in dispute over working hours and out-of-title duties, Dr. Richard A. Knutson, C.I.R. Chairman told MT. A ten-day atrike notice will go into effect March 15 unless an agreement is reached, Dr. Knutson said. Spokesman for the League, which halted talks with the C.I.R., refused comment ss "detrimental to our negotiations."

A.M.A. SUIT agsinat new utilization rsview procedures has surpriaed the government, HEW staffsrs told MT. Suit ssys HEW overstspped bounda by allowing non-MDs to servs on hoapital UR committees which must review Medicars/Medicaid caass within a day of sdmission. A.M.A. charges health care would bs endangered without acutally cutting costs. Rules went into effect Feb. 1, but hoapitals have until April 1 to comply.

Burrington Cites Clinitest Tablets' Peril to Children

By Thomas Bulger

Medical Tribune World Service

MONTREAL—Clinitest indicator tablets, used by the majority of the United States' 4,000,000 diabetics to determine urina sugar content, have been insufficiently recognized by physleians and patients as a serious hazard to small children, according to Dr. John D. Burrington, Professor of Surgery and Pediatrics at the University of Chicago Pritzker School of Medicine.

He reported to the annual meeting of the Society of Thoracic Surgeons here on five children between the ages of 19 and 26 months who incurred full-thickness burns of the esophagus after swallowing one of these tablets. All developed strictures that were re-

Continued on page 20

More Infarction, Less Pain

Angina Patient Mortality Not Cut by Surgery

By Frances Goodnight

Medical Tribune Staff

HOUSTON—Investigators who are conducting n randomized trial of medical vs. surgical therapy in 150 patients with unstable angina pectoris have found no difference so far in the mortality rates of the two groups, the American College of Cardiology was told here.

But in reporting on the eight-center cooperative study, Dr. C. Richard Conti, of the Johns Hopkins University School of Medicine, said its findings indicate that the medical and surgical patients differ in two areas of clinical concern—incidence of myocardial infarction and relief from pain.

Specifically, the incidence of myocardial infarction occurring in patients while still hospitalized or during the first year of follow-up has been "significantly greater" with surgery than with medical therapy, Dr. Conti said.

On the other hand, "a persistent anginal syndrome" has been observed more often in patients on medical therapy than nmong those treated by surgery.

The 150 patients with unstable angina taking part in the trial have hsd anginn of recent onset or a crescendo pattern associated with transient ECG changes. All have been admitted to a hospital because of a suspected impending myocardial infarction but candidates are excluded if a myocardial infarction occurred less than three months before admission.

Other grounds for exclusion from the study include appearance of new Q waves or evidence from enzyme determinations (made in the first 24 hours of hospitalization) that myocardial infarction has occurred. All accepted patients must be under 70 and must have a atate of health consistent with a further life expectancy of at least five years were it not for tha ischemic heart disease.

Dr. Conti also explained that patienta who are clearly better suited to one form of therapy than tha other ara excluded. Only those who satisfy clinical criteria ara asked to participate, and randomization takes place only if anatomy is judged suitable for bypass procedures.

Continued on page 3

Reaction to Edelin Conviction Is One of Shock and Dismay

Dr. Kenneth C. Edelin

By Sue Wymelenberg

Special Tribune Correspondent

BOSTON—Reaction to the conviction of Dr. Kenneth C. Edelin on the charge of msnslaughter has been one of dismay and shock in the medical community here.

Dr. Edelin, 36, was convicted of causing the death of a fetus during the performance of a legal abortion by hysterotomy in October, 1973, while

See One Man… and Medicine, page 15.

he was the chief obstetrical resident at Boston City Hospital. He was sentenced to one year's probation, stayed pending appeal. He is now free on a $100 bond.

Although the prosecution and the jurors insist that manslaughter, not abortion, was the issue, those in this community who are for and those who are against legalized abortion agree the conviction is a victory for the "right-to-life" movement.

Dr. Edelin's defense counsel, William P. Homans, Jr., commented as he and his client left the courtroom, "I would say that the vehemence with which the foreman shouted out the word 'guilty' shows something of the temper on tha part of the populace from which at least some members of the jury came."

Attorney Homans said that the case would be appealed, "even if the sentence is only a one dollar fine."

Dr. Edelin maintained that ha was not tried by a jury of his peers. "There are too many subtleties, too many complicated issues for people with no foundation in medicine to understand," he said in a television interview.

Assistant District Attorney Newman A. Flanagan, who prosecuted this case, will now move to preparations for a second trial in April, this one involving criminal charges against four other physicians at Boston City Hospital.

Their research on antibiotics effec-

Continued on page 3

'Blues' Battling For Life Against Takeover by US

By Linda Murray

Special Tribune Correspondent

For the first time in their history, Blue Cross and Blue Shield are fighting feverishly for their lives. "The future of Blue Shield . . . is by no means assured," warned Ned F. Parish, president of the National Association of

Second of a Series

Blue Shield Plana at the 1974 business meeting. The threat, of course, is national health insurance—which could either sweep the private sector aside entirely, or saddle it with a barrage of punitive restrictions.

To ward off a government takeover, the Blues have embarked on an intense program of house-cleaning and improved performance, emphasizing stepped-up cost control activities with some real grit and extensive involvement in the development of HMOs. Both moves promise to alter the Blues'

Continued on page 7

Medical Tribune Exclusive

MIPI Report on Adverse Drug Reactions

Medicine in the Public Interest (MIPI), a nonprofit, nongovernmental organization headed by Dr. Dana L. Farnsworth of the Harvard School of Public Health, recently published an extensive and objective study of reports of adverse drug reactions (ADR) by two leading pharmacologists, Drs. Fred Karch and Louis Lasagna, of the University of Rochester School of Medicine and Dentistry. Their 32-page report, reflecting the concern of leading physicians, has had virtually no coverage by the professional and lay media.

Because the MIPI study analyzes and reports on issues of importance to physicians in every branch of medicine, Medical Tribune is presenting highlights of some of the issues covered in the MIPI report.

THE MIPI STUDY of adverse drug reactions was stimulated by Senator Edward M. Kennedy's interest in obtaining objective expert evaluation of the problem. At hearings of his Senate Health Subcommittee some of the testimony offered resulted in frightening newspaper stories that presented an

First of a series

image of inept and ignorant physicians using powerful new drugs whose side effects harmed and killed scores of thousands of American patients. Nonresearchers extrapolated some data to estimate as many as 120,000 to 140,000 deaths, which excited the press and television news commentators.

Data . . . "Completely Unreliable"

After examining the data, Drs. Karch and Lasagna concluded that "current estimates of the magnitude and cost of the adverse reaction problem are completely unreliable." They cite its incomplete data base, its unrepresentative and uncontrolled character among its deficiencies. "No statistically valid estimates can be derived from such data. Therefore, "a moratorium on reckless statements and estimates" is "desperately" needed, they point out.

Failure To Include Outpatients

The MIPI report pointed out that one of the pitfalls in the existing literature was that "almost all surveys on the incidence of ADRs have limited their attention to hospitalized patients on acute medical wards. Such patients represent only a portion of the total hospital population, and the characteristics of this group may differ considerably from those of the whole hospital population."

Drs. Karch and Lasagna point out that ambulatory outpatients account for the greatest amount of medicinal use in United States. There simply has been "no systematic attempt to assess ADRs in outpatient population," a point which outlines a perspective considerably different than that created by press accounts. In fact, Drs. Karch and Lasagna go on to point out that the possibility of underprescribing or failing to prescribe drugs must be considered. "Noncompliance on the part of patients is usually in the direction of failure to take drugs; patients in pain are often understated in our hospitals; our hypertensive patients are often undertreated because they will not take medications that produce side-effects . . ." The problem requires "risk-benefit analysis," assert the investigators.

Drs. Karch and Lasagna urge the development of methods of gathering better, more complete data, including operational identification of drug reactions, a method for assigning a reaction causally to a specific drug, as well as the use of control groups, stratifications of populations and quantification of the benefits derived from drugs. They also recommend federal funding of a program addressed to these problems.

Well-Known Physicians In Leadership of MIPI

Most physicians do not know of Medicine in the Public Interest. It was "conceived for the purpose of conducting studies, performing analyses and making evaluations of present policies that the government cannot or will not perform and to do so in an objective fashion . . . so that policymakers and the public will be better informed. . . ."

Its Board of Directors is chaired by Dr. Dana L. Farnsworth. Other directors are: Dr. Daniel X. Freedman, Professor and Chairman, Department of Psychiatry, University of Chicago; Dean Charles O. Galvin, Southern Methodist University School of Law; Dr. Louis Lasagna, University of Rochester School of Medicine and Dentistry; Dr. Howard P. Rome, Mayo Clinic; Dr. Maurice H. Seevers, Professor and Former Chairman, Department of Pharmacology, University of Michigan; Dr. Chris Zarafonetis, Director, Thomas Henry Simpson Memorial Institute, University of Michigan.

DR. KARCH

DR. LASAGNA

Student Nurses Protest Training Cutback Plan

Student nurses, 1,800 strong, recently braved a snow storm and temperatures in the 20s in Albany to protest New York Governor Hugh Carey's plan to shut down a dozen nursing training programs at state hospitals.

Panelists Disagree on Issue Of How Much to Tell Patient

Medical Tribune Report

NEW YORK—How much truth should a patient be told? A Downstate Medical Center panel consisting of a rabbi, a psychiatrist, an internist, and a surgeon expressed sharp differences of opinion.

Although panel members concentrated on the problems of the dying patient, the moderator, Dr. Eli A. Friedman, Professor of Medicine, touched on the question of disclosure and information in more general terms.

"At Bellevue [Hospital]," Dr. Friedman said, "it has been shown that approximately 25 per cent of all medications are given in the wrong dose, or at the wrong time, or to the wrong patient."

"The only protection that the patient has against being dragged off to the wrong procedure, or having the wrong leg amputated, or being given the wrong medication," he declared, "is to know what the hell is supposed to be happening."

Dr. Friedman called for giving the patient more information in more situations than any of the other panel members.

"Truth is not for all people at all times," said Dr. Benjamin A. Rosenberg, Clinical Associate Professor of Medicine. "You have to individualize."

Jewish Law Cited

Rabbi Benjamin Z. Kreitman, Visiting Professor of Jewish Law at the Jewish Theological Seminary, tended to agree with this cautious approach. Applying religious law to the problems of the dying patient, Rabbi Kreitman said that if the patient "is a highly intelligent person with a strong character who is able to withstand any news, then you lead him in confession."

The Rabbi explained that leading the patient to confession is equivalent to telling him that his death is imminent. But confession is not mandatory, and, in fact, is "forbidden" in cases where the patient's peace of mind might be disturbed, he said.

The psychiatrist on the panel, Dr. Harold P. Surchin, said that the dy[ing] patient who has a history of depres[sion] should not be told he is dy[ing]. Nor would Dr. Surchin so inform [an] alcoholic patient.

He added, however, that "I gen[er]ally believe the patient always subcon[]sciously knows that he has a fatal ill[]ness."

The strictest rule was offered by Dr. Theodore R. Miller, Clinical Profes[sor] of Surgery at Cornell University Med[i]cal College in New York: "One mu[st] be authoritarian. I have never told [a] patient he was going to die."

Dr. Miller, who has been practic[ing] medicine for more than 40 years, t[old] the panel, "I have never had one ask."

New Test Predicts Leukemia Relapse

Medical Tribune Report

HOUSTON, TEXAS—A fairly relia[ble] test to predict relapse in leukemia pa[]tients in complete remission has bee[n] developed by physicians at M.D. Anderson Hospital and Tumor Institu[te].

Bone marrow cells from 25 adu[lt] patients, all of whom were in ap[]parently complete clinical remissi[on] from acute leukemia, were used to sti[m]ulate blastogenesis among autolog[ous] peripheral blood lymphocytes. Periph[]eral lymphocytes failed to react in 1[] patients, and 15 of these remained i[n] complete remission for a median time o[f] 10.5 months.

In the other two patients, and in th[e] of the eight whose peripheral blood lymphocytes were stimulated by th[e] bone marrow cells, remission ended a[t] a median of 6.5 months.

Dr. Jordan U. Gutterman sugges[ted] that use of the immunologic test to de[]tect minimal residual disease durin[g] apparent remission "should improv[e] the treatment strategy for patients wi[th] acute leukemia."

Dr. Gutterman's co-workers in th[e] study, reported in the *Journal of th[e] National Cancer Institute*, were Dr. Giora Mavligit, Michael A. Burgess, Kenneth B. McCredie, E.J. Freireich, and Evan M. Hersh, and Carol Hunter.

Reaction to Edelin Conviction: Shock, Dismay

Continued from page 1

tive against intrauterine infections set off the investigation of abortion practices at the city institution and resulted in their indictment and Dr. Edelin's.

The four doctors are David Charles, Leon Sabath, Leonard Berman and Agnets Phillipson.

Attorney Neil Chayet, who will represent Dr. Charles, said that he was very unhappy with the Edelin verdict, but not surprised.

"The thing that troubles me is that conviction is difficult, based on the evidence, and you begin to ask whether evidence really matters in these cases."

Both Mr. Chayet and Dr. Mitchell Rabkin, general director of Beth Israel Hospital, told MEDICAL TRIBUNE that the combination of the abortion issue, a black physician, and the present busing situation in Boston made a bad environment for deciding such emotionally-loaded issues.

'Unfortunate Fall Guy'

Dr. Kenneth Ryan, chief of staff of the Boston Hospital for Women and Chairman of the HEW Commission for the Protection of Human Subjects, pointed out that Dr. Edelin had complied with the law and with good medical practice.

"He has my personal confidence and support; he is just the unfortunate fall guy for society's battle, which belongs in the legislature, not the criminal court."

"I have been conservative on abortion, but I feel we have to defend women's rights and not force the will of one ethical or religious position on others who do not hold it," Dr. Ryan said.

The Association of Professors in Gynecology and Obstetrics, meeting in New Orleans, condemned Dr. Edelin's conviction, voting that "The adversary system of the criminal courts is not the place to define abortion, to define viability, or to define the moral issues of abortion. In our diverse society, we must guard against vocal jurisdictions or vocal minorities imposing their ethical positions on medical care, family planning, or abortion on those patients or doctors who do not hold these positions."

Dr. Edelin's status at the hospital is now unresolved. His case will be reviewed by the Boston Trustees of Health and Hospitals and the city's attorneys.

Dr. Edelin said he will continue to do abortions if he is permitted.

"I have not done anything which was illegal, absolutely nothing," he said. "I will continue to do abortions. They are a woman's right and it is better if they are done in a hospital setting by someone who is trained."

Indication of possible ramifications of Dr. Edelin's conviction came quickly. The District Attorney of New York's suburban Nassau County, Denis E. Dillon, said he would investigate a complaint by the Long Island Coalition for Life, an antiabortion group, that a fetus aborted at the Nassau Medical Center had been denied "all the ordinary medical means and reasonable efforts to preserve and protect life."

Dr. Louis Burke, director of clinical obstetrics at Beth Israel Hospital here, said the hospital will not change its basic policies on abortion, except those done by hysterotomy. In those cases, he told MEDICAL TRIBUNE, "we will have on tap life saving services in case the fetus is born alive. Since the conviction of Dr. Edelin for doing a hysterotomy, most of us fear this type of prosecution could happen to us. We will have spent thousands of dollars if there is even so much as a muscle twitch in the fetus to prove we did everything possible."

Dr. Ernest W. Lowe, chief of ob/gyn at Boston City Hospital, said there would be no change in that hospital's abortion policy, however.

Prosecution Definition

In the trial the prosecution defined abortion as the termination of pregnancy, but not necessarily involving the death of the fetus, and held that the physician has a responsibility to the fetus if there is a chance that it is viable.

Continued on page 13

Hemophilialike Ailment Seen In Women of 3 Generations

Medical Tribune Report

NEW ORLEANS—A bleeding diathesis indistinguishable from hemophilia A which has been transmitted as a dominant trait in women of three generations has been observed at the University of North Carolina.

Dr. E. S. Barrow described the anomaly to the Southern Society for Clinical Investigation here, reporting that there is nothing in the phenotype to suggest that the women are different from men with hemophilia A except the mildness of their symptoms.

The most striking abnormalities found in the laboratory are a reduction of Factor VIII to 2-12 per cent of control values, and a failure of *de novo* synthesis of Factor VIII to occur after transfusion, which is traditionally seen in van Willebrandt's disease.

The proband, first seen at North Carolina in 1954 at the age of 27, is the only one of the women to have a history of excessive bleeding. Her mother, born in 1898, is alive, well, and symptom free. Her daughter, born in 1946, has only a slight bleeding tendency. A granddaughter, born in 1972, has had a normal infancy without evidence of a bleeding tendency.

Dr. Barrow said six possible genetic mechanisms have either been excluded or tentatively ruled out by laboratory tests. These include a von Willebrand's disease phenotype; a previously described hemophilia A phenotype mutating at the Willebrand locus; extreme lyonization—i.e. random inactivation of almost all of the normal alleles in a heterozygote by being sequestered in Barr bodies; a balanced X-autosomal translocation occurring in a heterozygote for X linked hemophilia A; a dominant mutation at the hemophilia A locus in the X chromosome, and a dominant mutation at a previously unrecognized Factor VIII locus.

Angina Patient Mortality Not Cut by Surgery

Continued from page 1

Of the first 150 patients, 80 were randomly assigned to "vigorous medical management" and the other 70 similarly assigned to coronary artery surgery, Dr. Conti said. Both groups were similar from the standpoint of clinical presentation, clinical characteristics, age distribution, incidence of previous myocardial infarction, ECG changes, and coronary arteriographic disease.

Additionally, analysis of the left ventricular end-diastolic pressure, ejection fraction, and left ventricle contraction patterns did not reveal any significant difference between the two groups.

"Of the medical patients, two died while in hospital and three others died within the first follow-up year. Twelve experienced a nonfatal myocardial infarction—seven during hospitalization and five in the first year.

Among the 70 patients in the surgical group, three died in hospital and three more within the first year. A total of 20 developed a myocardial infarction—15 in the operative period or before discharge from hospital.

An actuarial survival curve plotted for the two groups indicates that projected survival of surgical patients after 12 months is 89 per cent, compared to 92 per cent for medical patients.

Information on relief from pain has been obtained by checking the symptomatic state of surviving patients in each group at the time of last follow-up.

Of the 75 medical-group survivors, 10 were subsequently considered "medical failures" by their physicians because of pain and were offered coronary artery surgery to relieve incapacitating anginal syndrome. All survived surgery but six have had a persistent anginal syndrome.

Only 33 of the other 65 medical-group survivors said they were free of pain. The remaining 32 reported an anginal syndrome with New York Heart Association Class 2 to 4.

By contrast, 56 of the 64 surgical-group survivors said they were free of pain.

Dr. Conti emphasized that the findings from the trial, which began in 1972, must be considered preliminary. The study is continuing at the eight participating centers: Johns Hopkins, Massachusetts General Hospital; University of Rochester, University of Chicago, Duke University, University of Alabama, Stanford University, and Cornell University.

index

CLINICAL NEWS NOTE: *"At Bellevue [Hospital], it has been shown that approximately 25 per cent of all medications are given in the wrong dose, or at the wrong time, or to the wrong patient. The only protection that the patient has against being dragged off to the wrong procedure, or having the wrong leg amputated, or being given the wrong medication, is to know what the hell is supposed to be happening." (Dr. Eli A. Friedman, see page 2.)*

feature index

Medical Tribune

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Exceptionally well absorbed oral broad spectrum antibiotic may be taken with meals

Larocin™ (amoxicillin) achieves high blood and urine levels

Low incidence of diarrhea to date in clinical studies

NUTLEY, N.J.—Roche Laboratories recently introduced an oral broad spectrum antibiotic: Larocin (amoxicillin). Larocin represents a significant contribution to antibacterial chemotherapy, one which will parform effectively in the treatment of a wide range of infactions due to sueceptibla organiams (eea chart at right).

Absorption called the key

The key pharmacologic charactaristic of Larocin (amoxicillin) is its rapid and efficient absorption from the gastrointestinal tract. Not only la it stable in stomach acid, but the presence of food has no eignificant effect on tha antibiotic'a abeorption. Thus Larocin may be taken by patiants on a conveniant *t.i.d.* schedule without regard to maals. The reconstituted oral suapension and padiatric drops may be added to liquids such aa formula, milk, fruit juice or aoft drinks for aasy administration to amall children.

Because of its efficiant absorption characteristice, high blood and urina lavele of Larocin (amoxicillin) are rapidly achieved. Peak sarum lavels avarage 4.2 mcg/ml two hours after a single 250-mg oral doea and 7.5 mcg/ml ona hour after a singls 500-mg oral dose—both levels approximately twice as high as those obtained with aqual doses of ampicilln.[1,2]

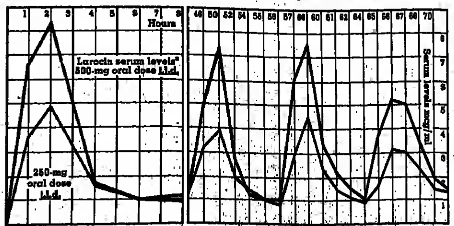
On a multiple-dose regimen, when given every eight hours for 8 deys, the lowest meen serum levels of Lerocin approximated 1.0 mcg/ml efter 250 mg and 1.25 mcg/ml after 500 mg.[3] Although the therapeutic renge of blood levels for the penicillins is not well esteblished, these results demonstrate that blood levels mey be expected to remain above the MIC's for all of the nonurinary pathogens susceptible to Larocin when it is administered at clinicelly recommended doses (eee chart bslow).

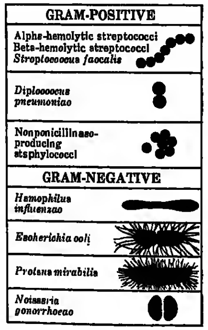
Most of Larocin ie excreted unchanged in the urine.[3] Average urinary excretion within 6 to 8 hours efter oral administration ranges from 40 to 79% for the 250-mg dose and 59 to 79% for the 500-mg dose.[1-5]

1. Croydon EAP, Suthorlend R: *Antimicrob Agents Chemother—1970*, pp. 427-430, 1971. 2. Nau HC, Winsholl EB: *Antimicrob Agents Chemother—1970*, pp. 423-426, 1971. 3. Data on file, Hoffmann-La Roche Inc., Nutley, New Jersey. 4. Leigh DA: *Curr Med Res Opin* 1:10-18, 1972. 5. Bodey GP, Nance J: *Antimicrob Agents Chemother* 1:358-362, 1972.

Hypersensitivity reactions can occur

As with other penicillins, it is anticipated that adverse reactions to Larocin (amoxicillin) will be largely limited to eensitivity phenomena. While anaphylaxis is rare in patients treated with oral penicillins, the possibility must nevertheless be kept in mind. Larocin is contraindicated in patients with a hietory of penicillin hypersensitivity. SERIOUS ANAPHYLACTOID REACTIONS REQUIRE IMMEDIATE EMERGENCY TREATMENT. (See Warnings section of complete product information, a summary of which appears at right.)





In vitro bactericidal activity

Note: Because Larocin (amoxicillin) does not resist destruction by penicillinase, it is not effective against penicillinase-producing bacteria such as resistant staphylococci. All strains of Pseudomonas and most strains of Klebsiella and Enterobacter are resistant.

Efficacy demonstrated in many infections

Amoxicillin has been administered successfully to patients with a wide range of commonly seen infections due to susceptible organisms.* Over-all clinical evaluation of amoxicillin therapy was conelderd a "success" or "improvsment" in 1267 of 1350 evaluable cases (93.8%).†

Ages of the 1350 patiants studied ranged from under ona year to over 80 years. Larocin capsules were administered to 800 patients and oral suspension to the remaining 550. Dosaga of tha capsulss ranged from 250 mg *t.i.d.* (the most frequantly used dosege) to a single 3-Gm dose for the treatment of acute uncomplicated gonorrhea. Dosage of tha oral suspension ranged from 50 mg *t.i.d.* to 250 mg *t.i.d.*, with 125 mg *t.i.d.* the most frequent. The majority of patients wera treated from seven to 10 days. A breakdown by type of infection follows:

Otitis Media: The pathogens most commonly isoleted were *Diplococcus pneumoniae* and *Hemophilus influenzae*. Of 130 cases with this diagnosis, 127 (98%) were rated es a "success" or "improvement" efter treatment with Larocin (amoxicillin).

* * *

Streptococcal Sore Throat: A success rate of 86% (174 of 202 cases) was observed with Larocin against the responsible pathogen, beta-hemolytic streptococci.† The great majority of the 202 patients in this group were children who received tha oral suspension.

* * *

Other Upper Respiratory Infections: Beta-hamolytic streptococci† were tha offending organisms for most of the infections in this group, which were diagnosed primarily es pheryngitis, with some casee of tonsillitis and a few cases of sinusitis. A success rate of 82% (56 of 68 cases) was achleved with Larocin.

* * *

Lowar Respiratory Infections: Treatmant with Larocin resulted in "success" or "improvement" in all of tha 52 cases in which *Diplococcus pneumoniae* was cultured. *Staphylococcus aureus* was also cultured in 26 of the 28 cases; Larocin showad "success" or "improvement" in 96% (25 of 26 caees). The most common clinical conditions were bronchitis and bronchopnaumonia.

* * *

Urinary Tract Infections: Cystitis, pyelonaphritis and asymptomatic bactariuria were the most frequent clinical diagnoses in thia group. Of the 404 cases evaluated, *Escherichia coli* was cultured in 306 cases and treatment with Larocin resulted in "succces" or "improvement" in 284 casaa (93%). *Proteus mirabilis* waa cultured in 70 patients, with Larocin effactive in 67 (96%).

* * *

Skin and Soft Tissue Infections: *Staphylococcus aureus* was cultured in 108 casea, with "success" or "improvamant" in 104 (96%); whila beta-hamolytic streptococci wera cultured in 99 ceses, with "success" in 97 (98%). Impetigo and abscesa wera tha most frequent diagnoses.

* * *

Gonorrhea: Administered as a singla 3-Gm oral dose, Larocin ehowed a succees rate of 97% in both males (85 of 88 cases) and femalea (114 of 118 cases).

**Data on file, Hoffmann-La Roche Inc., Nutley, New Jersey 07110.*
†"Success" or "improvement" was determined by a combination of clinical and bacteriological criteria. In infections due to beta-hemolytic streptococci and N. gonorrhoeae, only successes were included.

Low incidence of side effects reported to date

During tha clinical investigations with amoxicillin, all cases treated were avaluated for side effects. No sida effects or laboratory abnormalities which would be considered unusual for a penicillin derivativa wera reported by any of tha inveetigators.

In 2658 total courses of therapy with amoxicillin, therapy was discontinued in only 52 patients (1.9%) because of drug-related side effects. Laboratory abnormalitiee poesibly relatad to amoxicillin occurred infrequently.

Drug-Related Side Effects Associated with Amoxicillin

Based upon 2658 courses of therapy: 1811 with the capsules and 847 with the oral suspension.

SIDE EFFECT	CAPSULES #	CAPSULES %	SUSPENSION #	SUSPENSION %
Diarrhea	24	1.3	18	2.1
Rash	24	1.3	17	2.0
Nausea	7	0.3	1	0.1
Urticaria	6	0.4	2	0.2
Moniliasis	7	0.3		
Nausea/Vomiting	4	0.2		
Diarrhea/Nausea	3	0.1		
Vomiting	2	0.1	4	0.4
Dizziness	2	0.1		
Colitis	2	0.1		
Nausea/Headache	2	0.1		
Rash/Urticaria	2	0.1	1	0.1
Esophageal Spasm	1	0.05		
Stomachache	1	0.05	1	0.1
Belching	1	0.05		
Drowsiness	1	0.05		
Belching/Numbness/Tingling/Itching	1	0.05		
Fever/Itching	1	0.05		
Difficult Breathing	1	0.05		
Mucus in Pharynx	1	0.05		
Diarrhea/Urticaria	1	0.05		
Diarrhea/Vomiting	1	0.05	4	0.4
Dizziness/Headache	1	0.05		
Conjunctival Ecchymosis	1	0.05		
G.I. Bleeding	1	0.05		
Abdominal Cramps	1	0.05		
Diarrhea/Rash	1	0.05	1	0.1
Rash/Diarrhea/Vomiting			1	0.1
Sore Tongue			1	0.1
Rash/Vomiting			1	0.1
TOTAL	102	5.5	52	6.1

In these atudies, thara was a low incidanca of diarrhea reported with amoxicillin capsules—1.7% or 30 of 1811 patiants. Especially noteworthy was the low incidence of diarrhea reported with amoxicillin oral suspension—only 2.8% or 24 of 847 patients, significantly less ($p<0.05$) than the incidenca of diarrhea with ampicillin oral suspension (5.3% or 15 of 282 patiants).

In breaking down the over-all incidenca of diarrhea by age groups, it wae found that in the group from 0 to 1 (newborn and 1-year-old infants), 13 of 108 patients receiving amoxicillin oral suepension developed diarrhee, for an incidence of 12%. This represents over one-half tha total number of diarrhea cases seen in the 847 patients treated with amoxicillin oral suepension.

Throughout each of the remaining age categories, etarting from age 2 to 10 and in the general grouping from age 11 to 20, the incidence of diarrhea in patients treated with amoxicillin oral suspension ranges from 2% down to 0 in the older groups. There wera few cases of diarrhea beyond the age of aix.

The incidenca of diarrhea with Larocin (amoxicillin) can therefore be expected to be considerably higher in tha nawborn and infant age groups than in older children, which is true of all antibiotics.

Usual Adult and Pediatric Dosages

INDICATION	STRAIN ISOLATED	ADULT DOSAGE	PEDIATRIC DOSAGE*
Infections of the ear, nose, throat	Streptococci, pneumococci, nonpenicillinase-producing staphylococci, *H. influenzae*	250 mg t.i.d.	Oral Suspension: 20 mg/kg/day in divided doses t.i.d. Drops: Under 6 kg (13 lbs): 0.5 ml t.i.d.; 6-8 kg (13-18 lbs): 1 ml t.i.d.
Infections of the lower respiratory tract	Streptococci, pneumococci, nonpenicillinase-producing staphylococci, *H. influenzae*	500 mg t.i.d.	Oral Suspension: 40 mg/kg/day in divided doses t.i.d. Drops: Under 6 kg (13 lbs): 1 ml t.i.d.; 6-8 kg (13-18 lbs): 2 ml t.i.d.
Infections of the genito-urinary tract	*E. coli, Proteus mirabilis, Strep. faecalis*	250 mg t.i.d.	Oral Suspension: 20 mg/kg/day in divided doses t.i.d. Drops: Under 6 kg (13 lbs): 0.5 ml t.i.d.; 6-8 kg (13-18 lbs): 1 ml t.i.d.
Infections of the skin and soft tissues	Streptococci, susceptible staphylococci and *E. coli*	250 mg t.i.d.	Oral Suspension: 20 mg/kg/day in divided doses t.i.d. Drops: Under 6 kg (13 lbs): 0.5 ml t.i.d.; 6-8 kg (13-18 lbs): 1 ml t.i.d.
Severe infections, or infections caused by less susceptible organisms		500 mg t.i.d.	Oral Suspension: 40 mg/kg/day in divided doses t.i.d.
Gonorrhea, acute uncomplicated anogenital and urethral infections (males and females)	*N. gonorrhoeae*	3 grams—single oral dose	

*Note: Children weighing more than 8 kg (18 lbs) should receive the appropriate dose of the Oral Suspension; 125 mg or 250 mg/5 ml. Children weighing more than 20 kg should be dosed according to adult recommendations.

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Infections due to susceptible strains of the following gram-negative organisms: *H. influenzae, E. coli, P. mirabilis* and *N. gonorrhoeae*; and gram-positive organisms: streptococci (including *Streptococcus faecalis*), *D. pneumoniae* and nonpenicillinase-producing staphylococci. Therapy may be instituted prior to obtaining results from bacteriological and susceptibility studies to determine causative organisms and susceptibility to amoxicillin.

Contraindications: In individuals with history of allergic reaction to penicillins.

WARNINGS: SERIOUS AND OCCASIONALLY FATAL HYPERSENSITIVITY (ANAPHYLACTOID) REACTIONS REPORTED IN PATIENTS ON PENICILLIN THERAPY. ALTHOUGH MORE FREQUENT FOLLOWING PARENTERAL THERAPY, ANAPHYLAXIS HAS OCCURRED IN PATIENTS ON ORAL PENICILLINS. MORE LIKELY IN INDIVIDUALS WITH HISTORY OF SENSITIVITY TO MULTIPLE ALLERGENS. BEFORE THERAPY, INQUIRE CONCERNING PREVIOUS HYPERSENSITIVITY REACTIONS TO PENICILLINS, CEPHALOSPORINS OR OTHER ALLERGENS. IF ALLERGIC REACTION OCCURS, INSTITUTE APPROPRIATE THERAPY AND CONSIDER DISCONTINUANCE OF AMOXICILLIN. SERIOUS ANAPHYLACTOID REACTIONS REQUIRE IMMEDIATE EMERGENCY TREATMENT WITH EPINEPHRINE, ADMINISTER OXYGEN, INTRAVENOUS STEROIDS AND AIRWAY MANAGEMENT, INCLUDING INTUBATION, AS INDICATED.

Usage in Pregnancy: Safety in pregnancy not established.

Precautions: As with any potent drug, assess renal, hepatic and hematopoietic function periodically during prolonged therapy. Keep in mind possibility of superinfections with mycotic or bacterial pathogens; if they occur, discontinue drug and/or institute appropriate therapy.

Adverse Reactions: As with other penicillins, untoward reactions will likely be essentially limited to sensitivity phenomena and more likely occur in individuals previously demonstrating penicillin hypersensitivity and those with history of allergy, asthma, hay fever or urticaria. Adverse reactions reported as associated with use of penicillins: *Gastrointestinal:* Nausea, vomiting, diarrhea. *Hypersensitivity Reactions:* Erythematous maculopapular rashes, urticaria. *NOTE:* Urticaria, other skin rashes and serum sickness-like reactions may be controlled with antihistamines and, if necessary, systemic corticosteroids. Discontinue amoxicillin unless condition is believed to be life-threatening and amenable only to amoxicillin therapy. *Liver:* Moderate rise in SGOT noted, but significance unknown. *Hemic and Lymphatic Systems:* Anemia, thrombocytopenia, thrombocytopenic purpura, eosinophilia, leukopenia, agranulocytosis. All are usually reversible on discontinuation of therapy and believed to be hypersensitivity phenomena.

Dosage: *Ear, nose, throat, genitourinary tract, skin and soft tissue infections*—Adults: 250 mg every 8 hours. Children: 20 mg/kg/day in divided doses every 8 hours; under 6 kg, 0.5 ml of Pediatric Drops every 8 hours; 6-8 kg, 1 ml of Pediatric Drops every 8 hours. *Lower respiratory tract infections and severe infections or those caused by less susceptible organisms*—Adults: 500 mg every 8 hours. Children: 40 mg/kg/day in divided doses every 8 hours; under 6 kg, 1 ml of Pediatric Drops every 8 hours; 6-8 kg, 2 ml of Pediatric Drops every 8 hours. *Gonorrhea* (acute uncomplicated anogenital and urethral infections)—Males and females: 3 grams as a single oral dose. NOTE: Children weighing more than 8 kg should receive appropriate dose of oral suspension 125 mg or 250 mg/5 ml. Children weighing 20 kg or more should be dosed according to adult recommendations.

Note: In gonorrhea with suspected lesion of syphilis, perform dark-field examinations before amoxicillin therapy and monthly serological tests for at least four months. In chronic urinary tract infections, frequent bacteriological and clinical appraisals are necessary. Smaller than recommended doses should not be used. In stubborn infections, several weeks' therapy may be required. Except for gonorrhea, continue treatment for a minimum of 48-72 hours after patient is asymptomatic or bacterial eradication is evidenced. Treat hemolytic streptococcal infections for at least 10 days to prevent acute rheumatic fever or glomerulonephritis.

Supplied: Amoxicillin as the trihydrate: Capsules, 250 mg and 500 mg; oral suspension, 125 mg/5 ml and 250 mg/5 ml; pediatric drops, 50 mg/ml.

Larocin™ (amoxicillin)

an important contribution to oral broad spectrum antibiotic therapy

ROCHE

Therapy Helpful Even If Alcoholic Still Drinks

Medical Tribune Report

San Francisco—Even tbough treatment for alcoholism may not lead to nbstinence, it may hnve a significant rehabilitative effect, a two-year follow-up study haa shown.

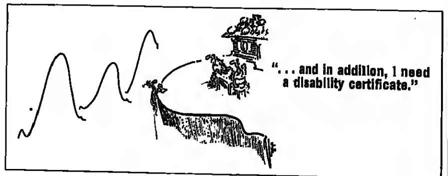
M. I. Kammeier, of the Hazledon Foundation, Center City, Minn., reported at the North American Coagress on Alcohol and Drug Problems that the lives of former patients bave improved, even if they still drink.

In their own evaluation and in that of persons close to them, former patients tend to be positive and optimistic, he said. The majority are happier and feel better nbout themselves than before treatment, the study found.

Questionnaires were sent to 143 former patients three and a half yeara after treatment, and data were obtained both from tbe 73 who returned the questioanaires and from persona close to the former patieats who could confirm drinking patterns.

Most of the former patients still drink, it was learned, but not ao frequently as before. Several, however, are drinking more than previously.

Mr. Kammeier noted that most of those who still drank do so in the same places, at the same time, and with the same beverages.



EDITORIAL CAPSULES

... brief summaries of editorials or comments in current medical and scientific journals.

On Virginia Apgar

"... Dcspite her fame from the Apgar score, she never anticipated that her name would become part of it. Nor was shc defensive sbout it. If someone were to suggest that the scoriag system had outlived its usefulness or shonld be revised, she would be the first one to agree.

"She had an extraordinary ability to ferret out the essentials and to cut into the core of a problem. She was the first person to catheterize the umbilical artery in a newborn infsnt ... the whole arca of newbom intensive cnre would not be where it is today were it not for Virginia.

"She achieved her greatest visibility in later years in her drive to educate the whole country about the aeed for early detection of birtb defects. She almost never turned down aa invitation to spenk, no matter how small or insignificant thc group, and her life became one long juggling act to fit speeches and site visits, professional consultations nnd chapter meetings, medla intcrvicws and international congresses Into her impossible schedule. Sbe waa the finest ambassador The National Foundatlon ever had. Undoubtcdly, she lifted birth defects from n secret cloaet and put them firmly on the map. ..." *(Commentary, L. Stanley James, M.D., Pediatrics 55:1 Jan., 1975)*

Home Care Ignored

"Health cnre profcssionals, third-pnrty paycrs, nnd government officials continue to extol the advantages of home care. Despite all the lip-service, however, wc are unlikely to witness any rapld overall expansion. Even where aome support is now avallsble, as under Medlcare, the relative use of home care continuea to decline year by year. For example, during 1969 there were 628,543 approved claims for home health services. ... By 1973, the number was down to less than 400,000 (based on the first 6 montha' experience).

"The reasons are not mysterious. Most physiciana are not interested in chronic illness. Most are not interested ln bome care, even if the visits are actually made by nurses. Most hospital administrators today are primarily concerned with keeping their expensive beds filled. And most third-party payars, public as well as private, are primarily concerned with keeping the physician and hospitals happy—or at least off their backs! Even the national government admlalstration, with its continual seolding of physicians and hospitals for rising costs, is onwilling or unable to exercise the leadership involved in a real reordering of national health prioritiea away from lnpatient eare toward the kind of program described by Dr. Brickner" [Ann. Int. Med. 82:1, Jan., 1975]. *(Editorial, Anne R. Somers and Nancy H. Bryant, R.N., M.P.H., Ann. Int. Med. 82:111, Jan., 1975)*

'Blues' Battle for Lives Against US Takeover

Continued from page 1

traditioaal relationships with hospitals aad physicians.

Back in October, Blue Cross Association president Walter McNerney announced n seven-part strategy to curb hospitalizatioa costs which all member plans were urged to adopt by July 1975. Although the announcement is certainly timed with an eye townrd public relations—in fact, none of the elements are new—it does mark the first time such a bald, ndversary position has been articulated at the nationnl level.

Prospective Reimbursement

Among tbe stipulations: that hospitals negotiate their prices in advance; more striageat use of utilization review of hospital admissions and stays to make sure every patient gets no more care than needed; requiring independeat auditors and full and regular disclosure by hospitals of their cost and accounting methods; and mandatory measures to prevent duplication of facilities and services.

Prospective reimbursement — the main thrust of the program—hns been voluntarily adopted by hospitals in only 15 plans so far, although some plans have had aeveral years experience with the technique. Blue Cross-Blue Shield of Greater New York, for example, has used prospective reimbursement since it was mandated by state law in 1969. Dr. Peter Rogatz, plan senior vice president, calls the technique "the main tool in increasing hospital efficiency" because the agreed upon rate "is what it would cost tbat hospital if it were operating at an efficient level. They won't get higher than that specified level from ua."

Proapective reimbursement hns n built-in incentive-pcnalty mechanism which works somewhat differently in different plans. "If the hospital is able to bring the coat in lower," explains Robert Schuler, vice president of Blue Cross of Western Pennsylvnnia, "It cnn keep half of the savings. If the eosts run over, the hospital is reimbursed one-half of every dollar that goes over tha prospective payments."

Efficacy Questioned

Bot questions have been raised about the efficacy of prospective reimbursement. "If the problem of riaing hospital costs were primarily one of inefficiency or incompetence, cost lncentives and penalties would be a helpful reform," writes attorney Sylvia Law, principal author of *Blue Cross: What Went Wrong?* "The basic isaues in cost control are questions of priorities, allocation of resources, and allocation of the power to make thesa judgmenta. New York's Cost Control Aet does nothing to affect these isaues. Hoapitals retaln unfettered freedom to effect savings or to limit the increase in costs in any way they see fit."

Bot tha Blues are attacking cost and quality control problems from a number of differeat angles at the same time and, ultimately, their efforts will have to ba evaluated cumulatively.

At the top of tho liat will be their development of Health Maintenance Organizations. Blue Cross currently tallies 53 HMOs that lt has helped launch and expects to expand that number to 280 by the end of the decade. Meanwhile, Blue Shield boasts 17 operational alternative delivery systems.

Such enthusiasm for the HMO concept has drawn the accusation from some quarters that the Blues are moving to dominate the HMO market. "Thnt's obviously not our intent," Walter McNerney snaps. "The HMO is a very important altcrnative in the market place and we want it to be there. We're sick and tired of everybody talking about HMOs and nobody doing them."

The prospect of the Blues dominating by default is not any more palatable to some observers lika Duke University Law Professor Dr. Clark Havighurst who thinks participation of health insurers in the HMO movements should be banned entirely. Quoted in *Blue Cross: What Went Wrong?*, Dr. Havighurst expressed fear that the Blues "might in some communities come to sell the bulk of the health insurance while also controlling the major HMO and reinsuring the competing HMOs against excessive risks."

Rochester, N.Y., Situation

In fnct, in Rochester, N.Y., the Gennessee Valley Group Health Association, developed by Bluc Cross/Blue Shield, with a $3 million health center, financed with Bluea' rcserves, "competes" with Health Watch, sponsored by the county medical society, and the Rochester Health Network, an nssociation of community health centers, both of which are underwritten by the Blues. In addition, the Blucs controlled 85 per cent of the market with standnrd covcrage prior to the HMOs' advent.

Since the HMO law stipulates that employcrs must offer HMOs if available ns an alternative form of health covcrage, thc qucstion has bccn raised of whcther n Blue Cross HMO nnd n Bluc Cross insurancc plan offered side by side meet the employcr's obligation. Dr. Havighurst thinks not. "It's not really an option," he says. "The purpose behlnd the lnw was to stimulste more competition. I would hope that tbe HEW regulations on HMOa clarify whether the employer can get by with these two ehoices."

But the employer may have little alternative. Private enterprise has been discouraged from entering the HMO market, some claim by the Blues themselves. In Philadelphia where Blue Cross serves as the underwriter snd fiscal intermediary for one HMO and has a close working relationship with anothar, Dr. Newton Speacer, Chairman of the board of Health Service Plan of Pennsylvania, a nonprofit corporation attempting to develop HMOs, claims obstruction by Blue Cross lncluding efforts to dissuade labor from switching over, and steadfsst refusal by tbe carrrier to work out a cooperative arrangement on hospital inaurance.

More generally, private enterprise is hampered by lack of access to markets, the need for a tremendous amount of capital and the pressures of a business that can't afford to grow alowly.

"HMOs aren't going to get off tha ground," predicts Walter McNerney, "nnless someone with our marketing expertise, contacts, and core of administrative people who know the health field and how to deal with out-of-aren benefits aad transfer rights ls willing to get lnvalved. Thnt's where Blae Cross caa play ane hell of a role."

But the Blues have plenty to learn. When the carriers attempted to market three HMOs alongside their own plan in Rochester, N.Y., initial enrollment for the trio was a meager one per cent of the market rather than the anticipated 20 per cent.

The problem: Not only was the standsrd coverage excellent, but the three new plans were marketed in a aeutral, disapassionate way without any advocacy. "Since we added a supplemental marketing force to push our product," relates Dr. Harold H. Gardner, Medical Director of the Genesee Valley Group Health Association, "aales have been going very well."

The Bluea are also learning things about marketing the concept to physicians. Although the carriers say they do not favor ane form of HMO over another, it is clear that the most appealing to doctors ia the foundation, open-panel type. "This does nothing to solve the access to care problem or come to grips with increased physician productivity," criticizes Leo E. Suycott, president of Blue Cross of Wisconsin, which has developed two closed-panel HMOs that have had so much difficulty with physician acceptance that Blue Cross is holding the line on development of any more HMOs until the problems can be worked out.

Open-Penel HMO Model

A major obstacle is the fact that Wisconsia is the showcase for what Blus Shield calls its Individual Practice Association model, an open-panel HMO with a combined eapitation nnd fee-for-service system, with 20 locations which hss attracted 97 per cent of the physicians in 22 countiea and a membershlp of 63,000.

"We feal lhis will have the most physician acceplance," snys participating internist Dr. Binka Waterhousa who ls promoting tha Health Maintonance Plan aroand lhe country. "It has the besl chanca of making an impnct on the delivery system. It's very much a patient-oriented program. It continues lo provide quality care without sacrificing any freedom of the patient to selecl, reject or changa physicians."

Then too, the fact that the driving force behiad it ls Blue Shield rather than Blue Cross may have something to do with it. "In Blue Shield aponsored HMOs," Len Caramela, Blue Shield's Director of Alternative Delivery Systems, feels, "there is greater potential for physician acceptance."

The Wlsconsia plaa, some observers feel, ls tha answer to the long-atanding problem of third party financing of routine office vlsits. "We have found that the physician is not really opposed to accepting third party money for primary care," notes Roger Graham, former director of research nnd planning at the Wisconsin Blue Shield plan. "Whst he ls really opposed to ls the idea of beiag employed by aome arbitrary outside iastitution."

At one time, according to Anne R. Somers, Associate Professor of Community Medicine at Rutgers Medical School, the Blues felt that HMOs would aave the private sector from annihilation or restriction at the hands of national bealth insurance. "They thought that if you could build competitioa in nnd get more managerial efficiency while keeping costs down, that there wouldn't be as much of a push for national hcalth insurance," sbe explaias.

Now the Blues see HMOs in a different context. "They might provide incrensed access once N.H.I. is a reality," speculates Mike Hcnry, Director of Alternative Delivery Systems for Blue Cross. "Considering the tremendous demand for services, HMOs can provide a higher level of access to care than can the regular system under this stress."

Role for Private Sector

Tbat's assuming that natioual health insurance will prescrve a rola for the private sector. Prof. Somers thinks it should. "But," she adds, "a limited role." Some of the controla sbe would like to see enacted are minlmum benefits standards, mandatory ambulatory covarage, and procedural safeguards for the insured with an appeals mechanism for rejected claims.

"By devising n plan tbat bas universal coverage but retnina soma controlled competitlon among a limited number of the better private carriera," she aays, "I think we can have the best of both worlda. And I think ll will come some day."

Mobile Isolator

A miniature space ault, developed by NASA, ls being tested as a prototype of an lsolation garment that may allow immuulty-deficlent children to leave their sterile habitats for a look at the outaide world. Filtered ventilation is provided by battery-powered blowera on an accompanying pushcart.

Botulism Outbreaks Rise

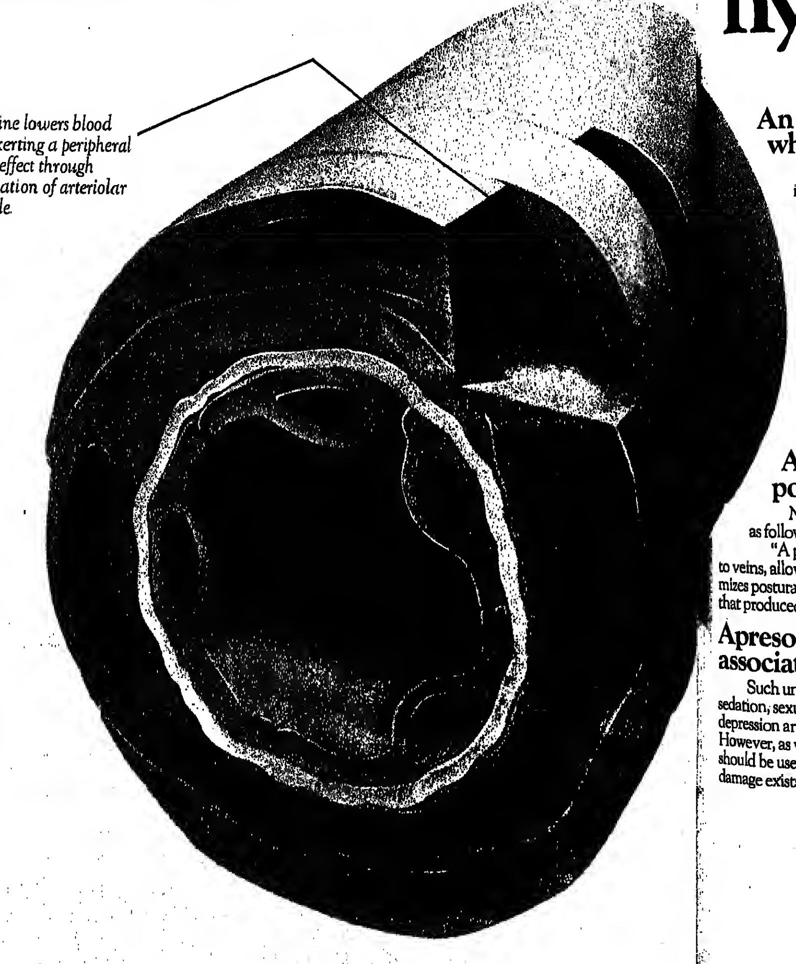
Medical Tribune Report

Atlanta, Ga.—Twenty outbreaks of foodborne botulism, involving 30 eases, were reported in 1974, the largest number of outbreaks siace 1935, according to the Center for Disease Control.

The C.D.C. aald the rise was probably related to an increase in home canning.

Apresoline® ...where the action is in treating hypertension
(hydralazine)

Apresoline lowers blood pressure by exerting a peripheral vasodilating effect through a direct relaxation of arteriolar smooth muscle.



An antihypertensive idea whose time has come

Doctors who treat hypertension are increasingly interested in the one oral drug that has a mechanism of action exclusively its own—Apresoline.

Apresoline is in an antihypertensive class by itself because it reduces blood pressure through a unique mechanism. Acting at the ultimate site of hypertension, it directly relaxes arteriolar smooth muscle to decrease peripheral vascular resistance and arterial pressure. As blood pressure falls, there is an accompanying rise in cardiac output and rate. Apresoline also maintains or increases renal and cerebral blood flow.

Apresoline minimizes postural hypotension

Nickerson[1] describes the action of Apresoline as follows:

"A preferential effect on arterioles, as compared to veins, allows the increase in cardiac output and minimizes postural hypotension; the latter is much less than that produced by agents blocking sympathetic nerves."

Apresoline avoids side effects associated with other agents

Such untoward reactions as drowsiness, lethargy, sedation, sexual dysfunction, and exacerbation of mental depression are not usually encountered with Apresoline. However, as with any antihypertensive agent, hydralazine should be used with caution where advanced renal damage exists.

Apresoline helps tailor the regimen to the patient

When Apresoline is added to an existing antihypertensive regimen, it introduces a different and complementary pharmacologic approach to the control of your patient's hypertension.

Apresoline thus affords the physician a variety of combinations with which he can construct regimens more closely molded to individual requirements. According to Freis,[2] such a combination of drugs, each with a different antihypertensive mechanism, is the most effective way to control blood pressure. This may also permit lower drug dosages.

Apresoline lends itself admirably to the contemporary antihypertensive rationale and its therapeutic goals: more vigorous and more effective control of blood pressure through a plurality of mechanisms.

Apresoline: used effectively in the VA studies

Apresoline was one of the three basic drugs used in two published VA cooperative studies.[3,4]

References: 1. Nickerson M: Antihypertensive agents and the drug therapy of hypertension, in Goodman LS, Gilman A (eds): *The Pharmacological Basis of Therapeutics*, ed 4. New York, The Macmillan Company, 1970, p 729. 2. Freis ED: Hypertension: a controllable disease. *Clin Pharmacol Ther* 13:627-632, 1972. 3. Effects of treatment on morbidity in hypertension: Results in patients with diastolic blood pressures averaging 115 through 129 mm Hg, Veterans Administration Cooperative Study Group on Antihypertensive Agents. *JAMA* 202:1028-1034, 1967. 4. Effects of treatment on morbidity in hypertension: II. Results in patients with diastolic blood pressure averaging 90 through 114 mm Hg, Veterans Administration Cooperative Study Group on Antihypertensive Agents. *JAMA* 213:1143-1152, 1970.

Next page: Apresoline (hydralazine) and the Hypertension Task Force

Apresoline® hydrochloride
(hydralazine hydrochloride)

TABLETS

INDICATIONS
Essential hypertension, alone or as an adjunct.
CONTRAINDICATIONS
Hypersensitivity; coronary artery disease; mitral valvular rheumatic heart disease.
WARNINGS
Chronic administration of doses over 400 mg per day may produce an arthritis-like syndrome leading to a clinical picture simulating acute systemic lupus erythematosus. This may also occur at *lower doses*. Most of these reactions are reversible upon withdrawal of therapy, but long-term treatment with steroids may be necessary *and residua* have been detected many years later. Complete blood counts, L.E. cell preparations and antinuclear antibody titer determinations are indicated before and periodically during prolonged therapy, even though patient is asymptomatic. These studies are also indicated in the presence of any unexplained symptoms.
Use MAO inhibitors with caution.
Usage in Pregnancy
The drug should be used only when, in the judgment of the physician, it is deemed essential to the welfare of the patient.
PRECAUTIONS
Use cautiously in suspected coronary artery or other cardiovascular diseases, cerebral vascular accidents, and advanced renal damage. Postural hypotension may occur, and the pressor response to epinephrine may be reduced.
Peripheral neuritis, evidenced by paresthesias, numbness, and tingling, has been observed. Published evidence suggests an antipyridoxine effect and addition of pyridoxine to the regimen if symptoms develop.
Blood dyscrasias, consisting of reduction in hemoglobin and red cell count, leukopenia, agranulocytosis, and purpura, have been reported rarely. If such abnormalities develop, discontinue therapy. Periodic blood counts are advised during prolonged therapy.
ADVERSE REACTIONS
Common: Headache; palpitations; anorexia; nausea; vomiting; diarrhea; tachycardia; angina pectoris. *Less frequent:* Nasal congestion; flushing; lacrimation; conjunctivitis; peripheral neuritis, evidenced by paresthesias, numbness, and tingling; edema; dizziness; tremors; muscle cramps; psychotic reactions characterized by depression, disorientation, or anxiety; hypersensitivity (including rash, urticaria, pruritus, fever, chills, arthralgia, eosinophilia, and, rarely, hepatitis); constipation; difficulty in micturition; dyspnea; paralytic ileus; lymphadenopathy; splenomegaly; blood dyscrasias, consisting of reduction in hemoglobin and red cell count, leukopenia, agranulocytosis, and purpura; hypotension; paradoxical pressor response.
DOSAGE
Initiate therapy in gradually increasing dosages; adjust according to individual response. Start with 10 *mg* 4 times daily for the first 2 to 4 days, increase to 25 *mg* 4 times daily for balance of first week. For second and subsequent weeks, increase dosage to 50 *mg* 4 times daily. For maintenance, adjust dosage to lowest effective level.
The incidence of toxic reactions, particularly the L.E. cell syndrome, is high in the group of patients receiving large doses of Apresoline.
In a few resistant patients, up to 300 mg Apresoline daily may be required for a significant antihypertensive effect. In such cases, a lower dosage of Apresoline combined with a thiazide, reserpine, or both *may* be considered. However, when combining therapy, individual titration is essential to insure the lowest possible *therapeutic dose of each drug.*
HOW SUPPLIED
Tablets, 10 mg (pale yellow, dry-coated); bottles of 100 and 1000.
Tablets, 25 mg (deep blue, dry-coated); bottles of 100, 500, and 1000.
Tablets, 50 mg (lilac, dry-coated); bottles of 100, 500, and 1000.
Tablets, 100 mg (peach, dry-coated); bottles of 100.

Consult complete literature before prescribing.

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C I B A

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Overmassage of Raw Data

At the 141st annual meeting of the American Association for the Advancement of Science, Mary L. Good, Ph.D., Boyd Professor of Chemistry at the University of New Orleans and a director of the American Chemical Society, referred to the overmassage of raw data by computer techniques. She was speaking at a symposium on "Responsibilities in the Use and Misuse of Scientific Data" and, in this instance, stated that some "currently utilized data reduction techniques are so intricate and complex that there is no doubt that in many cases data is synthesized and/or expanded beyond its reasonable expectation values by such computer techniques. It gets increasingly difficult to determine whether authors are reporting hard data or calculated data."

But even when data has not been calculated by computerized reduction techniques, it is not necessarily "hard." At the same symposium, Bernard L. Oser, Ph.D., former chairman of Food & Drug Research Laboratories, Inc., noted that "scientific data" in the strict sense means "observations and findings, which are generally expressed in numerical or descriptive terms." He then went on to observe that "even when correctly reported, 'data' are not necessarily equatable with 'facts.' Implicit in the latter term are the accuracy and reproducibility of findings and the competence and integrity of those responsible for the design, execution, and interpretation of the studies. Validity of the conclusions may depend on such critical factors as whether the right questions were asked, whether appropriate experimental conditions were used, and whether measuring devices or reagents were properly calibrated, to name a few."

So data, even observed measurements, is not necessarily hard, and not necessarily fact. Dr. Oser adds that "It is not uncommon, however, that differences found to be statistically significant on the basis of some arbitrary standard of comparison are intuitively believed to be unreasonable in the judgment of experienced investigators."

The disillusionment expressed by many scientists about the common misuse of scientific data was surely the stimulus for holding the symposium at the AAAS meeting. Dr. Good was disturbed by a failure "to clearly distinguish between scientific data which has been carefully measured or calculated and the opinions that we may have as to the significance of particular results to the public welfare." She emphasized that factual findings are repeatable by other workers but that "interpretation of that data in terms of its impact on society" is often debatable and subject to contrary emphases and opinions.

It is important to focus on the creditability of published data, on confidence limits and the hazards of drawing unrealistic conclusions. It is important to do so not only in regard to warnings about imminent hazards to our external macrobiosphere but also with regard to our internal microbiosphere as well. There is also the hazard that well-intentioned crying of wolf repeatedly—where there is no real wolf at hand—will ultimately create incredulity and disbelief when warnings are warranted and rational.

Anonymity

A proposal of extraordinary merit was recently made in the correspondence section of *Nature*. The letter writer suggested that "the best way to obviate the misuse of the unilateral anonymity granted to reviewers is to extend anonymity to authors as well. When the reviewers get a paper from the editor but have no idea who the authors are or what their affiliation is, they would find less pleasure in making unnecessary and uncivilized remarks. In addition, the reviewers would be able to judge a paper more justly and without prejudice."

So far, so good. But the letter writer took a giant step further and added "that all papers be not only reviewed but also published anonymously." He felt that this would reduce the number of unnecessary publications, diminish the "status" of being a prolific writer, etc., etc. But, doubtless, with that fatal additional proposal, he placed the kiss of death on his primary and meritorious suggestion. In effect he was requesting that scientists be saints or saintlike when, at best, they are human.

What is more, the letter itself was signed, casting doubts on the writer's own viewpoint.

Unstable Angina

Clinical Quote: *"A logical corollary from these observations is that the indications for surgery in patients with unstable angina may be the same as for patients with stable angina—that is, the relief of symptoms." (Dr. C. Richard Conti, et al, at American College of Cardiology,* *see page 1.**)*

"It's like inflation—too high."

LETTERS TO TRIBUNE

Reviewing Pension Reform

The article entitled "Pension Reform" by Charles Billman (MT, Oct. 2), includes a statement that is completely different from everything we have heard so far. It is so important a misstatement that I urge you to correct it immediately.

He states "The provisions that have the greatest impact on pension *and profit sharing plans* of professional corporations are:"

The differences between pension plans and profit sharing plans are enormous and the law applies only to pension plans. The law does not place the restrictions on profit sharing plans that he lists.

Unless he has information not available generally, perhaps it would be well to tell your readers what the situation really is in this important matter.

William F. Pollock, M.D.
Surgical Medical Group of Santa Monica, Inc.
Santa Monica, Calif.

In general, Dr. Pollock's thesis is correct, in that most of the provisions of the Pension Reform Act of 1974 do, in fact, relate to pension plans, rather than profit sharing plans. However, he is incorrect if he assumes that the Act does not impose new regulations with respect to profit sharing plans.

Act Section 3 (2) defines an "employee pension benefit plan" or "pension plan" to mean "any plan, fund, or program which was heretofore or is hereafter established or maintained by an employer or by an employee organization, or by both, to the extent that by its expressed terms or as a result of surrounding circumstances such plan, fund, or program provides retirement income to employees, or results in a deferral of income by employees for periods extending to the termination of covered employment . . .".

Therefore, the provisions of the Act do, in fact, enure to profit sharing plans as well as pension plans. Dr. Pollock should be advised that most of the troublesome provisions relating to funding, pension termination insurance, actuarial reporting, etc. do not apply to profit sharing plans.

Those provisions which do directly apply to *all* plans, including profit sharing plans are: reporting and disclosure; participation and vesting; fiduciary responsibility; administration and enforcement; deduction limitations; registration and information; and prohibited transactions, to name only a few.

We certainly hope that the above clarifies the application of the provisions of the Employee Retirement Income Security Act of 1974, with respect to profit sharing plans. It is our opinion that all professional corporations should review their existing pension and profit sharing plans in order to thoroughly review the amendments which *MUST* be made to all qualified retirement plans.

Charles R. Billman
President, Certified Plans
Newport Beach, Calif.

DWI and Penalties

Re your article on drinking drivers (MT, Nov. 6, 1974): As one who is concerned about the whole problem of alcoholism it seems to me after conviction, and in addition to other penalties, the car driven by the individual under the influence of alcohol should be impounded for several weeks. Impoundment could be applied to persons driving under the influence of drugs, or driving when license has been suspended.

Oklahoma has a law confiscating vehicles of persons convicted of poaching. However, the lawyers on the legislative council were cool to impounding cars for DWI (driving while intoxicated).

Roger Reid, M.D.
Ardmore, Okla.

H.E.W. Money-Saving

Your full page excerpts of Congressman Flood's talk at the Lasker Medical Research Awards Luncheon on "The Health Crisis in America Today" (MT, Dec. 11, 1974), winds up with the excellent invitation to advise him and his Sub-Committee on Labor and H.E.W. on ways for them to save money.

I therefore suggest to Congressman Flood—and his Subcommittee—that billions of taxpayers dollars can be saved by removing the ill-conceived Department of H.E.W. from our Public Laws because it has no legal basis for its existence under the Constitution of the U.S.A.

A. G. Blazey, M.D.
Washington, Ind.

Edelin Case a Reflection of Antiabortion Pressure

Medical Tribune Report

In accusing Dr. Edelin of manslaughter, the Commonwealth of Massachusetts reflected the angry pressures of the antiabortion forces in the state. Similar efforts are underway in other states as militant "right-to-life" groups seek legal status for the fetus, in order to discourage M.D.s performing abortions by making them subject to possible murder charges.

Dr. Edelin appeared to be a natural target for Boston antiabortion groups. As chief resident on the Boston University obstetrics and gynecology unit at Boston City Hospital, he and another physician had been doing most of the second trimester abortions there.

When the Supreme Court handed down its abortion decision in 1973, the number of women requesting abortions at the city hospital increased markedly, and then, in June, the bulk of physicians willing to do abortions finished their training and left B.C.H.

The new residents who came to the hospital in July generally refused to perform this service. Nine of the 13 were Roman Catholic and presumably had moral reservations. In addition, the procedures are considered uninteresting.

As a result, Dr. Edelin set up a special three-bed saline abortion unit within the hospital to handle second semester abortions as expediently as possible.

In a talk he gave before the trial

Courtroom Illustration: Robert J. Benson/WCVB-TV News

Dr. Edelin testified he would have had to twist awkwardly while keeping his hand in patient's uterus in order to watch clock for 3 min., as stale said.

began, he said that for some time he had felt under scrutiny by Massachusetts antiabortion groups.

Coincidentally in June, 1973, an article appeared in the *New England Journal of Medicine* describing research at B.C.H. on the efficacy of certain antibiotics in passing the placental barrier, using aborted fetal tissue.

Local antiabortionists immediately brought the article to the attention of the Boston City Council and demanded an investigation of the fetal research at the city facility.

Administrative Oversight

During his investigation, Assistant District Attorney Newman A. Flanagan received two anonymous telephone calls, informing him that two fetuses were being held in the B.C.H. morgue.

Both had been aborted in October by Dr. Edelin and, due to what was apparently an administrative oversight, they did not have death certificates as required by state law.

Mr. Flanagan decided to include Dr. Edelin in his investigation. He found that the fetuses were approximately the same gestational age and weight; one had been aborted by saline infusion, the other by hysterotomy.

Mr. Flanagan concluded that there was nothing incorrect about the fetus aborted by saline process because it had no chance to survive. The fetus delivered by hysterotomy, he concluded, was large enough to have been viable and its death implied criminal wrongdoing.

After several more months of investigation (MT, April 3, 1974) and a lengthy grand jury hearing in early 1974, the four physicians involved in the antibiotic research were indicted under an 1814 grave-robbing statute. Dr. Edelin was indicted for manslaughter.

He was not charged with illegal abortion. He was accused of causing a viable fetus to suffocate during the performance of a hysterotomy.

Dr. Edelin outlined what happened in the abortion this way in his testimony: In late September, 1973, a 17-year-old black woman came to the ob/gyn outpatient department at the hospital requesting an abortion. According to the date of her last menstrual period, she was approximately 18 weeks pregnant; examination by several of the house staff put the gestational age anywhere from 20 to 23 weeks.

Dr. Hugh Holtrup arranged for her admission for abortion by saline infusion; she was introduced to Dr. Edelin because he would be supervising the infusion.

Gestation '20-22 Weeks'

Several days later, on October 2, the patient was admitted to the saline unit where Dr. Edelin examined her. He testified that he "found the fundus one finger breadth above the umbilicus," and from this he estimated gestation at 20 to 22 weeks.

In trying to insert a needle into the amniotic cavity as a preliminary, he repeatedly drew blood. From this he made a presumptive diagnosis of an anterior placenta, so he tried to insert the needle from another point in the abdomen, with no success.

At this point he consulted with Dr. James Penza, co-director of the unit. Dr. Penza said he would try to start an infusion the next morning in the operating room; if he failed, Dr. Edelin would then proceed to do a hysterotomy.

Infusion Attempts Fail

Dr. Penza's infusion attempts did fail and Dr. Edelin went ahead with the surgery. To avoid the placenta he chose to make a small, vertical incision as low into the uterus as possible.

He testified that the incision was three or four centimeters, or just wide enough to accept two fingers, which he used to sweep along the walls of the uterus in an effort to loosen and remove "all the products of conception" intact.

This didn't work, the sac broke, and he was forced to grasp the fetal legs with his fingers and withdraw it, he told the court.

Dr. Edlin testified that he checked the fetus for signs of life and heartbeat, found none, and passed it to a basin held by the scrub technician before turning his attention back to his patient.

Dr. Enrique Gimenez-Jimeno had also examined the young patient when she was admitted and he found the fundus to be four finger breadths above the umbilicus, making her 24 weeks pregnant, he believed.

Dr. Gimenez-Jimeno appeared at the trial as the prosecution's star witness. A native of Mexico and a resident on the ob-gyn staff at B.C.H., he said he is sympathetic to the Right-to-Life movement, and refuses to do abortions.

He testified that he "couldn't believe" Dr. Penza and Dr. Edelin were going to abort a fetus he thought might be viable, so he made a point of observing the hysterotomy.

He told the court that he saw Dr. Edelin insert his "entire hand" into the uterus and make the vigorous motion designed to detach the placenta. "Then," he said, "with his hand still inside the uterus but not moving, Dr. Edelin waited for at least three minutes" while watching the operating room clock across the room.

If the fetus had been alive, Dr. Gimenez-Jimeno said, this would have prevented it from breathing.

After the three minutes had passed, he said, he saw Dr. Edelin remove the placenta and the baby," which showed "no signs of life."

This was the testimony on which the Commonwealth built most of its case.

All together, the Commonwealth called 14 witnesses in the effort to establish that the fetus was of a weight and gestational age to be viable, that it took a breath, and that birth actually takes place when the placenta is detached and the fetus is on its own.

Cross-examination by defense attorney Homans found that at least five of the prosecution witnesses were involved in the anti-abortion movement.

Directed Verdict Sought

After the prosecution rested its case on January 29, the defense presented a long and carefully researched argument in support of its request that the judge make a directed verdict. The basis of its argument was that the Commonwealth had not produced sufficient evidence that the fetus was viable to overturn the "live birth" rule.

Judge McGuire denied the request. The defense opened its case with the unusual strategy of calling the defendant to the stand as its first witness.

Dr. Edelin contradicted sharply some of the statements made by Dr. Gimenez-Jimeno. Asked by Mr. Homans about the placement of the clocks in the operating room—which his colleagun had accused bim of watching for three minutes—Dr. Edelin replied that the clock and timer were on the wall behind bim.

However, he added, "both of them had not been working for some time; in fact, to the best of my memory, they may have been out for repair that day."

He also explained that the anesthesia hook-ups dictated that a right-handed physician would have to stand with his back to the clocks.

Sweeping the accumulation of textbooks and notes from the long oak table used by the defense, Mr. Homans asked Dr. Edelin to demonstrate for the jury the position he would have had to take to watch the clock as Dr. Gimenez-Jimeno had testified, if his left hand was in the uterus.

To peer at the clock, which according to his testimony and photographs was behind his left shoulder, Dr. Edelin had to twist his body awkwardly away from the patient and crane his neck.

Whether Alive at Abortion

In his cross-examination, the assistant district attorney pressed the physician on the matter of whether or not the fetus was alive at the time of abortion. The physician said he had registered a fetal heartbeat of 140 three days earlier but did not check for heartbeat just prior to surgery.

Finally, Mr. Flanagan asked the young obstetrician whether or not he had a duty to protect the life of the fetus in an abortion.

His first duty is to the mother, not the fetus, Dr. Edelin replied. He said that attempting to save the life of a fetus he considers unable to survive is contrary to the purpose of abortion.

An obligation he might have to the fetus could only begin after its removal from the uterus, he told the court. "If in the eventuality that I ever delivered a liveborn fetus, then I would see that it was taken to the nursery. That has always been my philosophy."

Under further questioning, the obstetrician asserted he had never performed an abortion when he believed the fetus might be viable. "In fact, have refused to perform such abo tions."

After Dr. Edelin, the defense calle 15 more witnesses, 10 of them widel known as experts in their fields, t dispute the prosecution case point b point.

Dr. Gimenez-Jimeno's testimony about the clock-watching episode was contradicted by the nurse and the medical student who had assisted at the hysterotomy.

Breathing Denied

Two pathologists, Dr. Kurt Benirschke, Professor of Reproductive Medicine, University of California, San Diego and Dr. Arthur Hertig, Professor Emeritus of Pathology, Harvard, testified that on the basis of their microscopic examination of the fetal lung tissue the fetus never breathed air outside the uterus.

Experienced obstetricians, including Dr. R. Gordon Douglas, coauthor of "Operative Obstetrics," and Dr. Jack Pritchard, coauthor of "Williams on Obstetrics"—both texts used by the prosecution as references—testified that Dr. Edelin performed a routine hysterotomy according to good medical practice.

Drs. Douglas and Pritchard and other expert witnesses also supported Dr. Edelin's testimony that in an abortion the primary obligation of a physician is to the patient, not the fetus and supported the defense argument that abortion, by definition, implies the death of the fetus.

Dr. Jeffrey Gould, director of newborn services at B.C.H., called by the defense, told the court that in his opinion, the fetus was not of sufficient gestational age to live on its own. Except in rare instances, he said, viability occurs at about 28 weeks and 1000 grams.

The prosecution had placed the weight of the fetus at 700 gams, based on an autopsy performed by the county medical examiner four months after the abortion. Defense testimony put the weight at 600 grams, based on the examination of the B.C.H. pathologist hours after the abortion.

—S.W.

Reaction to Edelin Conviction Is One of Shock and Dismay

Continued from page 3

Dr. Edelin testified that he believes his primary obligation in an abortion is to the patient, not the fetus. His defense argued that abortion, by definition, implies the death of the fetus.

The Edelin case was at least the third legal attempt in recent years to establish that a fetus becomes a person not when it is removed alive from the uterus, but it is large enough and old enough to be viable.

Under common law, a fetus, viable or not, prior to being born alive has not been considered a "person" against whom a homicide can be perpetrated.

This is the so-called "live-birth rule" that evolved in law over the years, began in 1648, when Sir Edward Coke, Lord Chief Justice of England, wrote: "If a woman be quick with childe, and by a potion or otherwise killeth it in her womb, or if a man beat her whereby the childe dyeth in her body and she is delivered of a dead childe, this is a great misprison [misdemeanor] and no murder, but if the childe be born alive and dyeth of the potion, battery, or other cause, this is murder; for in law it is accounted a reasonable creature in 'rerum natura,' when it is born alive."

Dr. Edelin's defense attorneys—William F. Homans, Frank Sussman, and Jeanne Baker—also pointed out when they requested a directed verdict for acquittal early in the trial, on the grounds no crime had been committed, that in its 1973 Roe v. Wade abortion decision, "the Supreme Court held that the word 'person' as used in the 14th amendment does not include the unborn."

DR. EDELIN

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—S.W.

The helicopter—here, as seen later at low tide—was flown by an Air Force crew. None of the personnel on board were wearing heavy clothing and all felt half-frozen by the icy waters and biting wind.

Heroic Measures Save Infant in Downed Copter

WHAT STARTED OUT as a routine flight of the University of Oregon's neonatal emergency transport system recently ended with a plunge into an icy river and heroic measures by medical personnel to save the life of an infant. The *Health Sciences Center News* reported that 16-day-old Travis McCraw, in an isolette, was being flown to the center because of respiratory distress. Caring for the infant on board the helicopter were Dr. Raul Banagale and Joan Silbernagel, R.N. The baby was receiving oxygen and I.V. fluids when the engine of the helicopter failed. As the craft came down it struck a rock and fell on its side in the Columbia River. In almost total darkness and partly submerged, Dr. Banagale quickly removed the infant. Crew members helped the doctor and nurse wade through waist-deep water to a sandbar about 25 feet away. Crawling into a survival bag, Nurse Silbernagel took off her wet clothes and held the baby close to her body to keep him warm. An oxygen hose was slipped inside the bag and placed in front of the infant's nose, and dry Air Force socks were wrapped around him. The nurse recalls, "The only way to tell for sure if the baby was still alive was to hear him cry, so I kept pinching him." Rescued by another helicopter in about a half hour, the baby recovered quickly.

Travis McCraw appeared no worse for his experiences in the river. He was home in less than a week.

According to Dr. Banagale, shown with Nurse Silbernagel: "We didn't have time to get scared. Everyone's attention was on the baby. When you're so busy taking care of somebody, you don't have a chance to be afraid."

One Man...and Medicine

ARTHUR M. SACKLER, M.D.,
International Publisher, Medical Tribune

Doctor, are you innocent?

Doctor, are you innocent?

How many doctors can prove innocence, that they never did anything for which they could be charged with manslaughter—in the minds of some?

Dr. Kenneth C. Edelin of Boston had obviously been held innocent by a "jury of his peers," the medical staff of his hospital. Boston City Hospital brought no charge against him. He performed his duties in accord with the rules and regulations of the hospital and the dictates of his conscience as a physician. He was guilty of nothing except the performance of his duty. Dr. Edelin is as innocent of manslaughter as are most of his fellow physicians and as are the medical and other administrators of his hospital.

Yet Dr. Edelin was found guilty of manslaughter in standing by and denying a fetus oxygen and thereby causing its death.

Guilt and Injustice

There is guilt—the guilt of a society which permits a vicious manhunt against a physician performing his duties in accord with the rules of his hospital, the laws of the land, and the tenets of his conscience. There is guilt, and injustice, when an individual is unfairly singled out to be punished for an interpretation of law established only at his trial. If the medical profession remains silent, it too will share the guilt of hypocrisy which rapes the essence of justice.

Silence will open the doors wider for those "crusaders" whose only sensitivity is to the intensity of their own emotions without regard to the effect upon the rights, the beliefs and the freedom of their fellow citizens. And this goes for "crusaders" of the right as well as of the left. Silence by the "center," by the official and unofficial bodies of medicine, will be consent by neglect.

Dr. Edelin was found guilty of manslaughter in standing by and denying a fetus oxygen and thereby causing its death.

Who Else Denies Oxygen?

The cigarette manufacturers of America are guilty of negligence in these terms when the cancer-riddled lungs of a smoker deny him oxygen.

The newspapers and the advertising agencies of America are guilty of contributing to manslaughter in helping "push" oxygen-depriving carcinogens upon gullible people who want to be unbelieving.

Food manufacturers who load their products with sugar and saturated fats would join the cigarette makers in the difficult problem of trying to prove their innocence as to the cause of the epidemic disaster of American heart attacks which deprive their victims of essential oxygen—and of life itself.

Radio and television, which flooded the nation with the news of a doctor's conviction by a jury of his non-peers, might have to stand in the same dock with the newspapers—participants in an act of manslaughter by denying oxygen as a result of the damages of the products they promote.

The automobile manufacturers with their air-polluting engines and the owners of smoking, belching chimneys poison us with carbon monoxide and other disruptors of the oxygen carrying mechanism. They too can be subject to the charge of manslaughter on the same principle; they deny oxygen not just to one fetus but to mothers and their children, born and unborn, and the fathers as well.

Recognizing the True Issue

Let's get it straight.

I am against suicide. But I would be the last one on earth to deny an individual dying of an incurable and painful disease his right to confront the end of his life with what he believes to be dignity and peace.

I am deeply concerned about the population explosion but I am equally concerned with the attempt of governments to impose their policies by simplistic propaganda in support of sterilization and birth control techniques alone. I maintain the right of each individual to choose or not use contraceptive technology and/or abortion.

I am opposed to euthanasia. In this, too, I do not stand alone. The Catholic church, some of whose followers have pursued and persecuted Dr. Edelin, has recognized that there is a limit to "the artificial means," some of which stretch the limits of humanity, for keeping people alive.

Dr. Edelin Is Not Alone

Dr. Edelin does not stand alone in the dock. Doctor, you are there, too.

Dr. Edelin's actions were completely consistent with the rules and regulations, the practices and principles of one of the great hospitals of this country, Boston City Hospital. On the other hand, have you ever slipped? Has it ever happened that, wittingly or unwittingly and in good conscience, you have gone beyond what Dr. Edelin has done and broken the rules—and are guilty of manslaughter? Are you sure that you have always provided the necessary oxygen? Or all the other ancillary measures to assure that the patient has had the optimal cellular oxygenation?

As for the fetus, let us not forget that a highly dedicated physician who has devoted his life to the care of the pregnant woman and her child believes that a large section of the medical profession is guilty of mismanaging pregnancy in respect to salt and protein intake—that the fetal brain is damaged and that his approach to toxemia of pregnancy could save lives whose loss can be charged to other physicians as "manslaughter."

The Rule of Non-peers

The vulnerability of the medical profession is clearly evidenced in the rising tide of malpractice suits and judgments. There, juries of non-peers rule. The ultimate outcome is the present unreal situation with malpractice insurance rates. It should escape none that the resort to judicial processes in public climates which are constantly swayed by prejudice is no assurance that justice will be done. It would appear that the step from malpractice to manslaughter is a short one indeed.

Those who have made a nightmare of a physician's life, even as he began his practice of healing his fellowmen, can have you in the dock, too.

Have you interfered with the oxygen supply of a 24-week-old fetus? You are guilty. Of what? Of what is now described as a crime. Aren't you also guilty when interfering with the oxygenation of a ten-week-old fetus, or guilty of denying the ovum right to cellular oxygenation which is dependent upon fertilization?

Do you prescribe oral contraceptives? Are you sure you are innocent of a potential charge of manslaughter? "Right you are," I seem to hear the "right-to-life" people say. "That, too, is murder." They have the right to say so, but do they have the right to imprison you and me and others who do not agree with them? Could they get a "jury of peers" to convict? They did in Boston.

Not Only Right-to-Life Group

The danger posed is not limited to the "right-to-life" group. The crusaders of the left and many so-called libertarians make their fulsome contribution as they attack medical research on a "rights" basis. The populist drive on medicinal drugs with its distortions of medical history and therapeutic perspectives are part and parcel of the same thing—the tide of anti-science. Many good people as well as the Devil quote scripture. But let's not lift out of context "Love thy neighbor", "Judge not lest ye be judg

It was two years ago that I w
I would not wish to have my life h
in the balance of our judicial sy
(Med. Trib., Apr. 18, 1973). I h
that Dr. Edelin may yet be vindic
by higher judicial authorities who
penetrate the hypocrisy of our soci
the blindness of a jury of non-pe
and who will render a verdict of "
nocent"—the verdict which has be
rendered by the institution in whic
Dr. Edelin practices.

Oh, how right I was when I wrote,
"I cannot shake the lessons of history,
political as well as medical. I must
conclude that I, for myself or for a
member of my family, would prefer t
be at the mercy of the average prac-
ticing physician or average researcher
than to be medically or psychiatrically
at the mercy of either the state or of
its courts."

Minor Planet Honors Major Pathologist

Dr. Edward A. Gall, of the University of Cincinnati, has had a minor pl
named after one of his discoveries. The planet, first noted in 1916 but hith
nameless, has been officially designated Granule, to commemorate the
covery of a specific granule in lymphocytes by Dr. Gall and to honor his l
and distinguished career as a pathologist. Above, Dr. Gall at ceremo
honoring him upon retirement.

EPIGRAMS—Clinical and Otherwise

But in science the credit goes to the man who convinces the world, not to the man to whom the idea first occurs.

Sir Francis Darwin (1845-1925)
First Galton Lecture before the
Eugenics Society (1914)

"... I must be honest with you: I have assumed all this time that the hand was real."

Change in Sex Stereotypes Held 'Inevitable Tide of History'

By FRANCES GOODNIGHT
Medical Tribune Staff

NEW YORK—The change in male-femnle stereotypes now taking place in this country and elsewhere should be recognized as "not a matter of fashion or whimsy but an inevitable tide of history," a Johns Hopkins investigator declared here.

John Money, Ph.D., Professor of Medical Psychology, also said it is a mistake to believe that gender identity is so firmly fixed by nature prenatally that it is not "open to options of developmental differentiation."

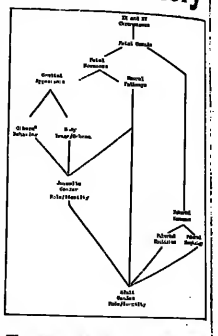
Some observers of today's scene argue thnt the idea of changing stereotypes of gender identity/role flies in the face of inmutable biology and the doctrine that anatomy is destiny, he told the American Assaciation for the Advancement of Sciease.

"But in actual fact," he said, "there is a series af bifurcations along the development pathway on which an individual personality becames gender-stereotypically imprinted. At any one of these bifurcations, *'nurture* may switch from male to female—or vice versa—the program that *nature* would otherwise have fallowed."

Discussing biasacial reasons for the change in sex stereotypes, Dr. Money cited five contributing determinants:

- The ioveation of labor-saving and augmenting machinery of the industrial and automation revolution, making male-female differences in size and strength less important nnd inctation and baby-care ability also less important.
- Extension of life expectancy, giving women extra years after childbearing and men nnd women extra years after childrearing.
- A lowering in the age of puberty, meaning thot women nny choose enrly childbearing with a later career or an early career with pastponement of children.
- The population explosion, with the need to limit family size.
- The development of effective, cheap, and mass-distributed means of birth control—aa inveation "as significant as the discovery of fire."

Dr. Money then summed up evidence for his conviction that "nurture can affect nature in the dimorphism of sexual differentiation."



The sequential action of the component variables of gender identity/role differentiation, according to John Money, Ph.D., of Johns Hopkins, who helieves thnt gender identity is not as firmly fixed by nature prenatally that it cnnnot he changed.

One clnssic exnmple of early prenatal environmental intervention, he snid, is the fertilized egg cell that is deprived by anme means of a Y chromosome.

"The embryo tlnt nature would otherwise huve programmnced to differentinte as a 46,XY chromosomal male thenceforth is programmed to differentinte ns a 45,X chromosomal female," he pointed ant. (The Y chromosome can be lust without destroying the cell's viability.)

Tho investigntor noted that this so-called Turner's syndrome has been recorded in one of a pair of monozygotic twins—one child was born with a penis, the other with a vagina.

The 'Adam Principle'

According to the "Adam principle," Dr. Money said, nature decrees that the sexually undifferentiated early embryo, whatever its genetic sex, will differentiate as a female unless androgen is added. And since the testis that supplies androgen is differentiated from neutral or ambisexual gonadal tissoes under instructioos from the Y chromosome, "the line of command is Y chromosome, testis, androgen."

Alteration of the prenatal environment at a critical period at any point in this line can thus prevent or arrest masculine differentiation, he said, allowing the "Eve principle" to take over.

Prenatal *non*masculinization of the external genitals of the sex-chromosomal male, and masculinization of the sex-chromosomal female, can both occur in human beings, Dr. Money continued. In the female, the usual cause is an excess of androgen supplied by the fetus's own adrenal cortices.

There is now behavioral evidence, he noted, that such prenatal androgenization of the sex-chromosomal female produces a disposition toward tomboyism, which is "compatible with a feminine differentiation of geader identity," not socially stigmatizing, and does not include "romantic nnd erotic lesbianism."

Althaugh fewer atudies hnve been possible on sex-chromosomnl males with an inaufficiency of the Adam principle, Dr. Maney said experiments with rats clearly indicate that feminine sexual behavior results from hormonnl nonmasculinization or submasculinization.

Discussing postnatal differentiation of gender identity/role, the investigntor emphasized his belief that sex differences programmed to take place after birth become incorporated as "indelibly" as those takiag place before birth.

"Dimarphism of behavior and imagery as masculine or feminine becomes programmed into the central nervous system as firmly as if it were genetically determined although, in fact, it is a product of early social interaction," he said, adding that the delivery-room announcement "It's a boy" or "It's a girl" will influence the baby's next 70 to 80 years.

Ta demonstrate the importance of early postnatal experience, Dr. Money cited his studies on 30 matched pairs of hermaphrodites in which each pnir was concordant for diagnosis and prenatal history but discordant for sex of assignment and postnatal history.

Markadly Different Outcomes

Both members of one pair were 46,XY chromosomal males, born with undescended testes and with an incompletely differentiated phallus. One was considered a boy at birth, assigned as a male, and giveo appropriate rehnbilitative surgical and pubertal-hormonal therapy. The other was thought to be a girl and given surgical and hormonal treatment accordingly.

The outcomes differed markedly, Dr. Money said. The girl differentiated a feminine gender identity/role and "is not remarkably different" from other women, including her romantic and erotic life, while the boy is now a married man with a professional career.

In anather case observed by Dr. Money, one of a pair of identical male twins lost the penis in a circumcision accident. The infant was promptly reassigned as a girl and in late childhood now has a gender identity/role "quite dimorphically different" from that of the brother.

"Cases such as these lead me to the conclusion that the irreducible sex differencea are that women menstruate, gestate, and lactate, and men impregnate," Dr. Money said.

Contrary to popular belief, he added, behavioral traits including aggression and parentalism are not sexually absolutely dimorphic even though the thresholds for their elicitation and the effective evoking stimuli may be sexually dimorphic.

"Most sexually dimorphic behavior as we know it is the product of cultural history and not of some eternal verity programmed by biology," he said. "As a people, we have a long history of maximizing sex differences in behavior rather than minimizing them. This is a policy that doubtless made good sense in neolithic times and later, but it is a policy which is not serving us very well today. It has become anachronistic."

In Dr. Money's view, if society decides to commit itself to a change of the sex stereotypes, the program must begin with childrenring. Gender identity/role has very plastic undifferentiated beginnings at birth, he poiated out, but differentiates in infancy and early childhaod "to have great tensile strength and resistance to reshaping, like steel that cools and hardens from the molten state."

Smallpox Cases Drop

Medical Tribune World Service

GENEVA—Only 1,400 cases of smallpox were reported last December throughout the world, according to the World Health Organization. The figure represents a decrease of almost 90 per cent from the total of 12,000 cases reported in December, 1973.

Wayne State Unit Operates 'Sickle Mobile'

The Camprehensive Sickle Cell Center at Wayne State University operates an unusual "Sickle Mabile" to perform many free services quickly and efficiently in different locatians. Staff members draw and test blaad (above), show an educational film, discuss blaad test results, and, if appraprinte, provide counseling.

Only one antihypertensive provides the three preferred modes of action...

Only Ser-Ap-Es combines control of fluid volume with hydrochlorothiazide

Hydrochlorothiazide provides a modest antihypertensive effect through control of extracellular fluid volume and potentiates the activity of other antihypertensive drugs.[5-7]

(a) Symbolized reduction in circulating fluid volume

plus control of sympathetic activity with reserpine...

Reserpine decreases blood pressure by interfering with the release of norepinephrine at peripheral sympathetic neuroeffector sites.[5-7]

Sympathetic inhibition also produces a central sedative effect especially useful in management of the stress-reactive patient.

(b) Schema of norepinephrine depletion at sympathetic nerve ending

plus direct relaxation of arteriolar smooth muscle with hydralazine...

The unique action of hydralazine lowers blood pressure through direct arteriolar vasodilation to reduce peripheral resistance.[5-7] The decrease in arteriolar resistance is accompanied by maintenance of regional vascular flow, making hydralazine particularly valuable for patients with slightly impaired renal flow.[7]

(c) Diagram of relaxed arteriole

...in a single tablet

Ser-Ap-Es®

reserpine 0.1 mg
hydralazine hydrochloride 25 mg
hydrochlorothiazide 15 mg

In treating hypertension, current clinical practice stresses the importance of achieving control of three basic homeostatic mechanisms: fluid volume, sympathetic activity, and arteriolar tone.[1]

Initial treatment most frequently employs one of the thiazides.[2-7]

But if blood pressure resists fluid volume control with thiazides, a second agent with a different mode of action, such as a sympathetic inhibitor (reserpine), may be gradually added.[2-4]

Many hypertensives, however, may resist control even with a two-drug regimen.

In such cases, the crucial "third step" in combined therapy is frequently control of arteriolar tone with hydralazine.[2-4]

Ser-Ap-Es combines all three steps in a single tablet—all the medication many hypertensives will need.

And when the dosage of each component corresponds to the dosages pre-established by individualized titration, Ser-Ap-Es may prove more convenient and more economical.

Doses of each component in Ser-Ap-Es are lower than when used alone.

Note: Use Ser-Ap-Es cautiously in patients with advanced renal damage or cerebrovascular accident. Discontinue at first sign of mental depression.

Ser-Ap-Es is the only antihypertensive agent that provides the three basic drugs used in two published VA cooperative studies.[8,9]

References: 1. Freis ED: Hypertension: a controllable disease. *Clin Pharmacol Ther* 13:627-632, 1972. 2. Even a little is too much. *Emergency Med* 5:144-185, 1973. 3. Bender AD, Familiar RG: Combination drug therapy in hypertension. *Del Med J* 40:5-8, 1968. 4. Bourne HR, Melmon KL: Guides to the pharmacologic management of essential hypertension. *Ration Drug Ther* 5:1-7, 1971. 5. Russell RP: Hypertension, in Harvey AM, Johns RJ, Owens AH, et al (eds): *The Principles and Practice of Medicine*, ed 18. New York, Appleton-Century-Crofts, 1972, pp 331-334. 6. Gifford RW Jr: Drugs for arterial hypertension, in Modell W (ed): *Drugs of Choice, 1972-1973*. St Louis, The CV Mosby Co, 1972, pp 390-393. 7. Sellers AM, Ilskovitz HD, Lindauer MO: Systemic arterial hypertension, in Conn HL Jr, Horwitz O (eds): *Cardiac and Vascular Diseases*. Philadelphia, Lea & Febiger, 1971, vol II, pp 934-943. 8. Effects of treatment on morbidity in hypertension: Results in patients with diastolic blood pressures averaging 115 through 129 mm Hg. Veterans Administration Cooperative Study Group on Antihypertensive Agents. *JAMA* 202:1028-1034, 1967. 9. Effects of treatment on morbidity in hypertension: II. Results in patients with diastolic blood pressure averaging 90 through 114 mm Hg. Veterans Administration Cooperative Study Group on Antihypertensive Agents. *JAMA* 213:1143-1152, 1970.

Ser-Ap-Es®

reserpine 0.1 mg
hydralazine hydrochloride 25 mg
hydrochlorothiazide 15 mg

INDICATIONS
Based on a review of this drug by the National Academy of Sciences-National Research Council and/or other information, FDA has classified the indications as follows:
Effective: Hypertension. (See box warning.)

WARNING
This fixed combination drug is not indicated for initial therapy of hypertension. Hypertension requires therapy titrated to the individual patient. If the fixed combination represents the dosage so determined, its use may be more convenient in patient management. The treatment of hypertension is not static, but must be reevaluated as conditions in each patient warrant.

CONTRAINDICATIONS
Reserpine: Known hypersensitivity; mental depression (especially with suicidal tendencies); active peptic ulcer; ulcerative colitis; electroconvulsive therapy.
Hydralazine: Hypersensitivity; coronary artery disease; mitral valvular rheumatic heart disease.
Hydrochlorothiazide: Anuria; hypersensitivity to this or other sulfonamide-derived drugs. The routine use of diuretics in an otherwise healthy pregnant woman with or without mild edema is contraindicated and possibly hazardous.

WARNINGS
Reserpine: Use with extreme caution in patients with a history of mental depression. Discontinue at first sign of despondency, early morning insomnia, loss of appetite, impotence, or self-deprecation. Drug-induced depression may persist for several months after drug withdrawal and may be severe enough to result in suicide. MAO inhibitors should be avoided or used with extreme caution.
Hydralazine: Chronic administration of doses over 400 mg daily may produce an arthritis-like syndrome simulating acute systemic lupus erythematosus. This may also occur at *lower doses*. Long-term treatment with steroids may be necessary and residua have been detected many years later. CBC's, L.E. cell preparations, and antinuclear antibody titer determinations are indicated before and periodically during prolonged therapy with hydralazine or if the patient develops any unexplained signs or symptoms. Use MAO inhibitors with caution.
Hydrochlorothiazide: Use with caution in severe renal disease. In patients with renal disease, thiazides may precipitate azotemia. Cumulative effects of the drug may develop in patients with impaired renal function.
Thiazides should be used with caution in patients with impaired hepatic function or progressive liver disease, since minor alterations of fluid and electrolyte imbalance may precipitate hepatic coma.
Thiazides may be additive or potentiative of the action of other antihypertensive drugs. Potentiation occurs with ganglionic or peripheral adrenergic blocking drugs.
Sensitivity reactions are more likely to occur in patients with a history of allergy or bronchial asthma.
The possibility of exacerbation or activation of systemic lupus erythematosus has been reported.

Usage in Pregnancy
Reserpine: The safety of reserpine for use during pregnancy or lactation has not been established; therefore, the drug should be used in pregnant patients or women of childbearing potential only when, in the judgment of the physician, it is essential to the welfare of the patient. Increased respiratory tract secretions, nasal congestion, cyanosis, and anorexia may occur in neonates and breast-fed infants of reserpine-treated mothers since reserpine crosses the placental barrier and appears in maternal breast milk.
Hydralazine: The drug should be used only when, in the judgment of the physician, it is deemed essential to the welfare of the patient.
Hydrochlorothiazide: Usage of thiazides in women of childbearing age requires that the potential benefits of the drug be weighed against its possible hazards to the fetus. These hazards include fetal or neonatal jaundice, thrombocytopenia, and possibly other adverse reactions which have occurred in the adult.

Nursing Mothers
Thiazides cross the placental barrier and appear in cord blood and breast milk.

PRECAUTIONS
Reserpine: Use cautiously in patients with history of peptic ulcer, ulcerative colitis, or gallstones (biliary colic may be precipitated).
Exercise caution when treating hypertensives with renal insufficiency. Use cautiously with digitalis and quinidine.
Intraoperative hypotension has occurred in hypertensive patients receiving rauwolfia preparations, but withdrawal of reserpine does not assure that circulatory instability will not occur in such patients.
Hydralazine: Use cautiously in suspected coronary artery or other cardiovascular disease, cerebral vascular accidents, and advanced renal damage. Postural hypotension may occur, and the pressor response to epinephrine may be reduced.
Peripheral neuritis, evidenced by paresthesias, numbness, and tingling, has been observed. Published evidence suggests an antipyridoxine effect and addition of pyridoxine to the regimen if symptoms develop.
Blood dyscrasias, consisting of reduction in hemoglobin and red cell count, leukopenia, agranulocytosis, and purpura, have been reported. If such abnormalities develop, discontinue therapy. Periodic blood counts are advised during prolonged therapy.
Hydrochlorothiazide: Periodic determination of serum electrolytes to detect possible electrolyte imbalance should be performed at appropriate intervals. Observe patients for clinical signs of fluid or electrolyte imbalance (hyponatremia, hypochloremic alkalosis, and hypokalemia). Serum and urine electrolyte determinations are particularly important when the patient is vomiting excessively or receiving parenteral fluids. Medication such as digitalis may also influence serum electrolytes. Warning signs are dryness of mouth, thirst, weakness, lethargy, drowsiness, restlessness, muscle pains or cramps, muscular fatigue, hypotension, oliguria, tachycardia, and gastrointestinal disturbance such as nausea or vomiting.
Hypokalemia may develop with thiazides as with any other potent diuretic, especially during brisk diuresis, when severe cirrhosis is present, or during concomitant administration of steroids or ACTH.
Interference with adequate oral intake of electrolytes will also contribute to hypokalemia. Digitalis therapy may exaggerate metabolic effects of hypokalemia especially with reference to myocardial activity.
Any chloride deficit is generally mild and usually does not require specific treatment except under extraordinary circumstances (as in liver disease or renal disease). Dilutional hyponatremia may occur in edematous patients in hot weather; appropriate therapy is water restriction rather than administration of salt, except in rare instances when the hyponatremia is life-threatening. In actual salt depletion, appropriate replacement is the therapy of choice.
Transient elevations in plasma calcium may occur in patients receiving thiazides, particularly in those with hyperparathyroidism. Pathological changes in the parathyroid gland have been reported in a few patients on prolonged thiazide therapy.
Hyperuricemia may occur or frank gout may be precipitated in certain patients. Insulin requirements in diabetic patients may be increased, decreased, or unchanged. Latent diabetes may become manifest during thiazide administration.
Thiazide drugs may increase the responsiveness to tubocurarine. The antihypertensive effects of the drug may be enhanced in the postsympathectomy patient. Thiazides may decrease arterial responsiveness to norepinephrine. This is not sufficient to preclude effectiveness of the pressor agent for therapeutic use.
If nitrogen retention indicates onset of progressive renal impairment, consider withholding or discontinuing diuretic therapy.
Thiazides may decrease serum PBI levels without signs of thyroid disturbance.

ADVERSE REACTIONS
Reserpine: *Gastrointestinal*—hypersecretion; nausea; vomiting; anorexia; diarrhea. *Cardiovascular*—angina-like symptoms; arrhythmias (particularly when used concurrently with digitalis or quinidine); bradycardia. *Central Nervous System*—drowsiness; depression; nervousness; paradoxical anxiety; nightmares; rare parkinsonian syndrome and other extrapyramidal tract symptoms; CNS sensitization (manifested by dull sensorium, deafness, glaucoma, uveitis, and optic atrophy). *Miscellaneous*—frequently nasal congestion; pruritus; rash; dryness of mouth; dizziness; headache; dyspnea; syncope; epistaxis; purpura and other hematological reactions; impotence or decreased libido; dysuria; muscular aches; conjunctival injection; weight gain; breast engorgement; pseudolactation; gynecomastia; rarely water retention with edema in hypertensive patients.
Hydralazine: *Common*—headache; palpitations; anorexia; nausea; vomiting; diarrhea; tachycardia; angina pectoris. *Less frequent*—nasal congestion; flushing; lacrimation; conjunctivitis; peripheral neuritis, evidenced by paresthesias, numbness, and tingling; edema; dizziness; tremors; muscle cramps; psychotic reactions characterized by depression, disorientation, or anxiety; hypersensitivity (including rash, urticaria, pruritus, fever, chills, arthralgia, eosinophilia, and, rarely, hepatitis); constipation; difficulty in micturition; dyspnea; paralytic ileus; lymphadenopathy; splenomegaly; blood dyscrasias, consisting of reduction in hemoglobin and red cell count, leukopenia, agranulocytosis, and purpura; hypotension; paradoxical pressor response.
Hydrochlorothiazide: *Gastrointestinal*—anorexia, gastric irritation, nausea, vomiting, cramping, diarrhea, constipation, jaundice (intrahepatic cholestatic), pancreatitis. *Central Nervous System*—dizziness, vertigo, paresthesias, headache, xanthopsia. *Dermatologic-Hypersensitivity*—purpura, photosensitivity, rash, urticaria, necrotizing angiitis, Stevens-Johnson syndrome, and other hypersensitivity reactions. *Hematologic*—leukopenia, agranulocytosis, thrombocytopenia, aplastic anemia. *Cardiovascular*—orthostatic hypotension may occur and may be potentiated by alcohol, barbiturates, or narcotics. *Other*—hyperglycemia, glycosuria, hyperuricemia, muscle spasm, weakness, restlessness. Whenever adverse reactions are moderate or severe, reduce dosage or withdraw therapy.

DOSAGE
As determined by individual titration (see box warning).
Usual dosage is 1 or 2 tablets t.i.d. For maintenance, adjust dosage to lowest patient requirement. When necessary, more potent antihypertensives may be added gradually in dosages reduced by at least 50 percent.

HOW SUPPLIED
Tablets (dark salmon pink, dry-coated), each containing 0.1 mg reserpine, 25 mg hydralazine hydrochloride, and 15 mg hydrochlorothiazide; bottles of 100 and 1000.
Consult complete literature before prescribing.

CIBA Pharmaceutical Company
Division of CIBA-GEIGY Corporation
Summit, New Jersey 07901

C I B A

Clinitest Hazard to Small Children Stressed

Continued from page 1

fractory to repeated dilation and required resection.

The deleterious substance appears to be the 233 mg. of sodium hydroxide that, in normal urine testing, provides two essential requirements for the indicator reaction: a strongly basic pH and, by its heat of hydration, temperatures that are close to the boiling point.

When a tablet is swallowed by a child, Dr. Burrington said, it apparently dissolves in saliva to a sludge that sticks in the esophagus about the level of the carina and causes a severe burn, both by its caustic nature and by the large local release of heat. A stricture then develops over the ensuing three to four months.

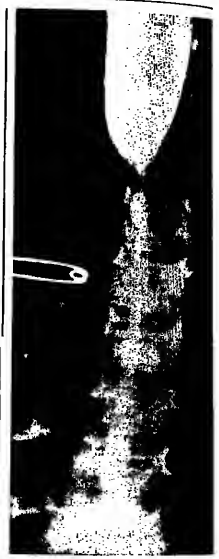
Dr. Burrington said that his experience demonstrates that both patients and their physicians are insufficiently acquainted with the hazards of these tablets. In one case, the child's father saw him swallow the table but was unaware of the danger and so did not seek medical help until the next day, when the child was febrile, tachypneic, and unable to swallow his saliva. Radiographic studies at the hospital showed a right upper lobe pneumonia and, on barium swallow, narrowing of the esophagus at the level of the carina.

Dysphagia of 2 Weeks' Duration

In another case, a child was brought to the hospital with dysphagia of two weeks duration. Although persistent questioning of siblings eventually enabled the physician to relate the symptoms to Clinitest ingestion, neither he nor the parents had been aware of the tablets' caustic nature.

All five patients had strictures sufficiently short for resection and end-to-end anastomosis of the esophagus to be accomplished without disruption of the diaphragmatic crura or the cardioesophageal junction. Although four of the five also required dilatations postoperatively, all but one are now eating normally.

Dr. Burrington noted that vinegar and lemon juice are listed as antidotes on the bottle, but expressed the belief that they may do more harm than good. While it seems logical to neutralize the caustic base with these acids, he said, the neutralization reaction intensifies the release of heat and probably potentiates the thermal component of the burn.



Barium swallow shows short, tight esophageal stricture in a two-year-old three weeks after ingestion of single Clinitest tablet. Dr. Burrington says the tablets have been insufficiently recognized as a hazard to children.

The preferred antidote, he said, is cold milk, which also has the advantage of being readily available and acceptable to the child. He suggested a flush of tap water as a second choice.

While the use of steroids and antibiotics is generally thought to be helpful in the treatment of sodium hydroxide burns of the esophagus, he remarked, only one of the five patients was seen by a physician early enough for this therapy to be instituted. The acute symptoms are often surprisingly mild, he said, so that the child may not be brought to the physician's attention until the developing stricture seriously interferes with swallowing.

The possibility of Clinitest ingestion should therefore be considered with any child who presents with a short, persistent esophageal stricture, Dr. Burrington commented. He added that the absence of diabetics in the child's immediate family should not rule out this explanation, since two of the five children he treated swallowed the offending tablet while visiting in another home.

The problem is compounded, he observed, by the fact that the simple screw-top bottles containing the tablets, whose flecked appearance is apparently attractive to children, are often left in easily accessible places—the back of commodes, for example—in order to be convenient for urine testing. As with any dangerous substance, they should be stored in child-proof containers out of easy reach, he said.

Clinical Trials by Oldden

TRIBUNE SPORTS REPORT

Doctors Are Urged to Take Keener Interest in Ski Safety

Medical Tribune Report

PORTLAND, ORE.—Physicians can help curb the estimated 600,000 ski-related injuries that will occur on U.S. slopes this year, an authority on alpine skiing told the 16th National Conference on the Medical Aspects of Sports here.

Eugene Bahniuk, Ph.D., Associate Professor of Biomedical Engineering and Assistant Professor of Orthopedics at Case Western Reserve University, said that an estimated 5,000,000 Americans will do some skiing this year and that physicians should take an interest in their safety education.

At least 50 per cent of the skiing injuries reported each year are equipment-related, Dr. Bahniuk said, and the rest can be chalked up to poor physical condition or ignorance.

"Physicians, especially those in areas where skiing is popular, can contribute a lot to the over-all safety of the sport by cautioning patients against poor physical conditioning and equipment hazards," he said.

Muscle Role Is Primary

"Physical conditioning plays a major role in the severity of a ski-related injury. Certainly, energy-absorption ability of bone is very small, so the skier's primary defense mechanism is muscular conditioning. This suggests that better physical conditioning provides better energy absorption, thereby offering the skier more protection. . . .

"Doctors can help a lot just by familiarizing themselves with various aspects of ski equipment, such as bindings. . . .

"It is particularly important that children's ski bindings not be considered in the same category as toys. Children have a higher incidence of ski injuries than adults, and the consequences of injury to the epiphyseal plate are uniquely serious."

The average binding for a child is technically inferior to the average one for an adult, and physicians in areas where skiing is popular should be aware of this, Dr. Bahniuk said.

He also commented on hazards presented by ski poles, runaway devices, and improper clothing:

• Ski poles have been implicated in shoulder dislocations, thumb dislocations, and lacerations.

"Ski poles may be caught in a stationary object, such as a tree branch, and because of the straps which are so commonly used, the skier's hand will remain stationary with the pole as the skier's body continues in its original direction of motion."

Pull-away straps are needed to avoid the possibility of dislocation when that happens, and physicians should tell their patients so.

• Runaway devices have two basic forms. Some are straps that attach the skier to the ski. Other forms are mechanical devices that react with snow to prevent a ski from sliding down the slope after the binding has been released.

"Runaway straps have flaws. After the ski has released, the runaway strap keeps the released ski in the region of the skier. Fallen skiers have been incented by the sharp edges of the released ski."

• Improper clothing can be another hazard, of which few skiers, and even fewer physicians, are aware.

"Ski clothes have been directly implicated in ski injuries. Ski clothes should have a high coefficient of friction when in contact with snow and ice. In some falls it is only the frictional resistance of the skier's clothes which provides a deceleration force," he said.

DL-Norgestrel, a New Form, Efficacious in Canada Study

BY BEN ROSE
Medical Tribune World Service

WINNIPEG, MAN.—An oral contraceptive with a low dose of estrogen (30 micrograms) and 300 micrograms of DL-norgestrel, a new form of progestin, has proven efficacious in blocking ovulation in a series of 23 women, it was reported here to the annual meeting of the Royal College of Physicians and Surgeons of Canada.

The study was described by Dr. Earl Plunkett, Professor and Chairman of Obstetrics and Gynecology, University of Western Ontario, London, Ont.

The women received three months of medication spaced between a month with no medication. Dr. Plunkett said all the subjects were then regular in ovulation.

Mid-period bleeding, occurred in 10 to 15 per cent of the patients in the first month, 10 per cent in the second, and 5 per cent in the third.

Dr. Plunkett also noted the work of other investigators of the drug who have described a significant drop in cholesterol level of subjects. He said a minor change in the molecular structure of progestin alters its metabolic effects significantly, and predicted this would be a fruitful area of research.

Rand Manpower Study

Medical Tribune Report

SANTA MONICA, CAL.—Bigger money and high prestige draw California medical students into the specialties and the cities, and away from the longer working hours, poor health services, and lower pay of rural areas, according to a study by the Rand Research Corporation.

The study recommended more physician training for people from rural areas, television and computer link-ups between urban and rural health services, and redistribution of educational funds on a statewide basis.

Medicine on Stamps

Theodor Billhsrz

Born in Sigmsringen, Germsny, in 1825, Bilhsrz received his medicsl education at the Uoiversity of Tubingea. In 1850 he emigrated to Cairo snd becsme interested in Egyptisn entozoa. In 1851 he discovered a blood fluke snd later its eggs in the urine of pessants suffering the hematuria and bladder calcification of schistosomisals, or bilhsrziasis.

Text: Dr. Joseph Klar
Stamp: Minkus Publications, Inc., New York

IMMATERIA MEDICA

From 3 K's to 3 F's

Dr. M. W. L. Davis, who is in family practice in Regins, Saskatchewsn, had some fun reviewing *Is Marriage Necessary?* by L. Casler, Ph.D., in the January *Canadian Family Physician*. Noting that Dr. Cssler proposed "evolutionsry" development of "permissive mstrimony," Dr. Davis went on to say: "His hesitation to propose the extreme position is mstched by his reluctance to take the ultimate step with langusge. He avoids the evolution of female function from the 3 K's (kinder, kuche and kirche)—to the 3 F's ss 'feeding, flattering, and sexual ioter-course' (sic)!"

Obviously, it's a case of the alphabet-syndrome. Just for starters in F, we'll throw out a few: fakiog, fooling, feeling, frenzy, and fun.

Changing Concepts

We're indebted to Dr. Raymond M. Dorsch, Jr., of Lebnnon, Pa., for the following item from the *Philadelphia Inquirer's* medical column:

"The pelvic exomination is important tsnt to evsluate the size of the uterus, its position, or the presence of any runnors of the uterus or ovsries."

Not a solo practice, Immateria Medica welcomes contributions from readers. Send them to Immateria Medica, MEDICAL TRIBUNE, *880 Third Avenue, New York, N.Y. 10022. Tonight, that is.*

A spiky fever.
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